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The Impact of Antenatal Azithromycin and Monthly Sulphadoxine-Pyrimethamine on Child Mortality, Morbidity, Growth, and Development

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Abbreviations and Acronyms

AZI	azithromycin
AZI-SP	intervention group receiving sulphadoxine-pyrimethamine monthly and azithromycin twice
CI	confidence interval
cm	centimeter
g	gram(s)
HAZ	height-for-age z-score
Hb	hemoglobin
HIV	human immunodeficiency virus
kg	kilogram(s)
LAIS	Lungwena Antenatal Intervention Study
MUAC	mid-upper arm circumference
NS visit	non-scheduled visit
SD	standard deviation
SP	sulphadoxine-pyrimethamine
under-5	child under 5 years of age
WAZ	weight-for-age z-score
WHZ	weight-for-height z-score
WHO	World Health Organization

Executive Summary

Background. Public health interventions targeting childhood growth failure and undernutrition have been largely based on the promotion of a healthy diet and effective infection control in early childhood. Recently there has been increased attention to the fetal period and its critical importance for subsequent health. However, there is a relative paucity of empirical data on the impact of pregnancy interventions on child health beyond immediate birth outcomes.

A randomized, controlled trial conducted in rural Malawi from 2003–2006 provided an opportunity to study medium-term effects on children after interventions targeted to pregnant women. The trial enrolled 1,320 pregnant women in three intervention groups. Participants in the control group received standard Malawian antenatal care, which included intermittent preventive malaria treatment in pregnancy with sulphadoxine-pyrimethamine (SP) once at enrollment and once between 28–34 weeks of gestation. Participants in the monthly SP intervention group received SP monthly from enrollment until 37 weeks of gestation. Participants in the azithromycin (AZI)-SP intervention group received monthly SP and two doses of active AZI (once at enrollment and once between 28–34 weeks of gestation) to eradicate possible maternal reproductive tract infections and strengthen the antimalarial effect of SP.

As a follow-up to the trial, we tested the hypotheses that children born to mothers treated during pregnancy with monthly SP, with or without two doses of AZI, would have a lower number of deaths during the first 5 years of life, a lower incidence of non-scheduled (NS) visits to the health center during the first 3 years of life, be taller and otherwise larger in size through the first 5 years of life, and have a higher total developmental score at 5 years of age than children born to mothers who received standard malaria treatment in pregnancy.

Methods. Primary outcomes of the follow-up study were the number of deaths by 5 years of age, the incidence of NS visits by 3 years of age, child length/height at 2 and 5 years of age, and total developmental score at 5 years of age. For mortality outcomes, we calculated total mortality during the first 5 years of life, number of miscarriages and stillbirths, number of early and late neonatal deaths, number of postneonatal deaths, and number of child deaths. We used the number of NS visits as a proxy for morbidity because we did not have direct data on child morbidity. Child anthropometrics were measured at the age of 1, 3, 6, 9, 12, 15, 18, 24, 30, 36, 48, and 60 months. We calculated age- and sex-standardized anthropometric indices (height-for-age z-score, weight-for-age z-score, weight-for-height z-score, head circumference-for-age z-score, and mid-upper arm circumference [MUAC]-for-age z-score) by using the World Health Organization Child Growth Standards. Values below -2 z-scores were considered indicative of stunting, underweight, wasting, small head circumference, and low MUAC. Child development was measured at 5 years of age with Griffith's Mental Development Scale. We calculated total developmental score as a sum of locomotor, personal-social, language, eye and hand coordination, performance, and practical reasoning subscale scores.

For mortality outcomes and the prevalence of various forms of malnutrition, we calculated percentages and risk ratios. We calculated incidence rate ratios for the total number of NS visits. For anthropometric indices and developmental scores, we calculated group means and differences between groups. We used log-binomial regression models to estimate risk ratios for binary end-points at a single time point and negative binomial regression adjusted for time in follow-up to estimate incidence rate ratios for total number of NS visits. We used least squares regression to calculate differences in means for continuous outcomes.

Developmental results were adjusted for child age at the time of developmental assessment and child sex, otherwise all main results are shown without covariate adjustments. As a sensitivity analysis, we also estimated coefficients adjusted for a set of covariates. All regression models for the mortality and morbidity outcomes were adjusted for the same set of covariates, based on whether the potential covariate was associated with any mortality or morbidity outcome at $p < 0.05$. All regression models for anthropometric outcomes were adjusted for the same set of covariates, selected based on covariate selection carried out with 24-month outcomes. All regression models for total developmental score were adjusted for covariates associated with total developmental score at $p < 0.05$.

As exploratory analyses we also tested for the presence of an interaction between the intervention and pre-specified maternal and child characteristics. We performed analyses stratified by the respective variables if the interaction term was significant at $p < 0.1$. The purpose of the interaction testing was exploratory rather than confirmatory.

Results. The proportion of children who died during the follow-up was 15.3% in the control group, 15.1% in the monthly SP group, and 13.1% in the AZI-SP group ($p = 0.603$). The proportion of postneonatal deaths was 5.5% in the control group, 3.3% in the monthly SP group, and 1.9% in the AZI-SP group ($p = 0.008$ AZI-SP vs. control). The incidence of NS visits during the first 3 years of life was 0.12 in the control and monthly SP groups and 0.13 in the AZI-SP group ($p = 0.710$). The mean height-for-age z-score was higher in the AZI-SP group than in the control or monthly SP groups at all time points. Mean absolute length/height in the AZI-SP group was 0.4–0.7 cm higher compared to the control group between 1 and 60 months. The AZI-SP group also had a higher mean weight-for-age z-score and head circumference-for-age z-score compared to the control and monthly SP groups at all time points. Differences between groups in mean weight-for-height z-score were not consistently in favor of AZI-SP or any other intervention group over time. Mean MUAC-for-age z-score was higher in the AZI-SP group compared to the control group from 6 to 36 months of age, but at 48 and 60 months, those differences had disappeared. The mean (standard deviation [SD]) total developmental score was 108.8 (17.1) in the control group, 110.3 (17.0) in the monthly SP group, and 112.5 (17.6) in the AZI-SP group ($p = 0.029$), with the AZI-SP group having a 3.7 point higher score compared to the control group ($p = 0.008$). Covariate adjustment did not markedly change these results. Although effect modification was observed for some outcomes, the results did not show a clear pattern in how the effect of the intervention was modified by maternal background variables or child characteristics.

Conclusions. The results of this study support the hypothesis that children born to mothers who receive monthly SP and two doses of AZI during pregnancy are on average taller throughout the first 5 years of life than children born to mothers who receive standard malaria treatment in pregnancy. It is also possible that differences in newborn weight and head size are sustained for 5 years but this was not conclusively confirmed. The results also support a positive effect of the AZI-SP intervention on postneonatal infant mortality and the developmental status of the children at 5 years of age. The results do not support the hypothesis that the intervention would reduce child morbidity during the first 3 years of life in rural areas of Malawi.

1 Introduction

Traditionally, public health interventions targeting childhood growth failure and undernutrition have been largely based on the promotion of a healthy diet and effective infection control in early childhood (ACC/SCN 2001; Victora et al. 2010). Recently, however, there has been increased attention on the fetal period and its critical importance for subsequent health. Many policy documents guiding future public health interventions have been based on the concept of the "first 1,000 days." Such documents emphasize that the foundations of good health are laid during the fetal period and the first 2 years of life (Piwoz et al. 2012), and as such, effective public health interventions should target this age window. Thus far, however, there is a relative paucity of empirical data on the impact of pregnancy interventions on child health beyond immediate birth outcomes.

Researchers from the University of Malawi and the University of Tampere conducted a randomized controlled trial in rural Malawi from 2003–2006. The trial, known as the "Lungwena Antenatal Intervention Study" (LAIS), provided an opportunity to study the medium-term effects on children after an intervention targeted to pregnant women. The study involved a total of 1,320 pregnant women who were randomized to one of three interventions: (1) standard antenatal care (two doses of sulphadoxine-pyrimethamine [SP] for the prevention of malaria); (2) monthly SP; or (3) monthly SP supplemented with two doses of azithromycin (AZI), an antibiotic to help reduce the burden of malaria and maternal infections. In the study sample, women treated with monthly SP and two doses of AZI during pregnancy had an approximately 35% lower incidence of preterm delivery and babies with low birth weight than women in the control group who received only two doses of SP (12% vs. 18% for preterm delivery, 9% vs. 16% for low birth weight) (Luntamo et al. 2010). A similar positive effect was seen in the prevalence of neonatal stunting; 15% of the babies born to mothers in the intensive infection treatment group were stunted at 1 month of age compared to 24% in the control group (Luntamo et al. 2013).

The results from the LAIS trial suggest that child birth size can be increased with intensive infection control during pregnancy. However, it is not clear whether the effects can be sustained during childhood. With nutrition interventions during pregnancy, the impact is often lost within a year after birth (Ashorn et al. 2015; Lanou et al. 2014). The aim of the current study was to determine if children born to mothers treated with monthly SP with or without two doses of AZI would be larger in size at 2 and at 5 years of age than children born to mothers in the control group. The aim was also to determine the effect of the intervention on child mortality during the first 5 years of life, child morbidity during the first 3 years of life, and child development at 5 years of age.

2 Methods

2.1 Study Design, Outcomes, and Ethics Statement

This study was a 5-year follow-up to the LAIS trial, a single-center, randomized, partially placebo controlled, outcome assessor-blinded, three-arm clinical trial conducted in rural Malawi. In this follow-up study, child morbidity was assessed during the first 3 years of life, child mortality and growth during the first 5 years of life, and child development at 5 years of age. The hypotheses of the follow-up study were that children born to mothers who were treated during pregnancy with monthly SP, with or without two doses of AZI, would have a lower number of deaths during the first 5 years of life, would have a lower incidence of non-scheduled (NS) visits to the health center during the first 3 years of life, would be larger in size (length/height, weight, head circumference, and mid-upper arm circumference [MUAC]) at 2 and 5 years of age, and would have a higher total developmental score at 5 years of age than children born to mothers in the control group.

The original LAIS trial hypothesis was that maternal antibiotic treatment with monthly SP alone or in combination with two doses of AZI improves fetal growth and decreases the incidence of preterm delivery, and that this leads to increased infant size at birth and at 1 month of age. The primary efficacy and safety outcome measures were the incidence of preterm delivery and serious adverse events. The main secondary outcomes were mean newborn size (weight, length, and head circumference) at birth and at 28 days of age as well as the prevalence of underweight, stunting, and wasting at 28 days of age.

Both the original trial and the follow-up were performed according to Good Clinical Practice guidelines and the ethical standards of the Helsinki Declaration. The protocol was approved by the College of Medicine Research and Ethics Committee, Malawi and the Ethical Committee of Pirkanmaa Hospital District, Finland. An independent data safety and monitoring board monitored the incidence of suspected serious adverse events, conducted one site monitoring visit, and performed two interim analyses for safety and efficacy. Only participants who signed or thumb-printed an informed consent form were enrolled in the study. Key details of the protocol were published at the clinical trial registry of the National Library of Medicine in Bethesda, MD, United States (http://www.clinicaltrials.gov, trial identification NCT00131235).

2.2 Study Site and Participants

The study enrolled women with uncomplicated second trimester pregnancies (gestational age 14–26 weeks by ultrasound assessment) who had felt the movements of the fetus, were available during the follow-up period, and started antenatal care between December 2003 and October 2006 at Lungwena Health Centre in southern Malawi. Exclusion criteria included severe illness, receipt of AZI during the current pregnancy or SP within the preceding 28 days, allergy to study drugs, and any previous serious allergic reaction. The last follow-up visit for children born to the women enrolled in the study was completed in June 2012.

2.3 Study Interventions

Participants in the control group received standard Malawian antenatal care, which included intermittent preventive treatment in pregnancy with SP (three tablets orally, each containing 500 mg of sulphadoxine and 25 mg of pyrimethamine) twice: at enrollment and between 28–34 weeks of gestation. At these visits, they also received a placebo to azithromycin. Participants in the monthly SP intervention group received SP monthly from enrollment until 37 gestational weeks and a placebo to azithromycin. Participants in the

AZI-SP intervention group received monthly SP and prophylactic treatment with active AZI (two tablets orally, each containing 500 mg of AZI) twice: at enrollment and between 28–34 weeks of gestation. All participants received ferrous sulphate (200 mg/day) and folic acid (0.25 mg/day) throughout pregnancy (supplied by Malawi Central Medical Stores). SP tablets were purchased from Malawi Central Medical Stores, supplied by Pharmanova (Blantyre, Malawi), Ipca Laboratories Ltd. (Mumbai, India), F. Hoffmann-La Roche Ltd. (Basel, Switzerland), and Universal Corporation Kenya Ltd. (Kikuyu, Kenya). Active AZI and its placebo were manufactured and donated by Pfizer Inc. (New York, United States).

2.4 Randomization and Enrollment

A researcher not involved in data collection generated a randomized code list. Based on this list, individual code slips containing unique identification numbers, but not group allocation, were sealed in individual opaque randomized envelopes. An individual drug box was pre-packed for each identification number. It contained appropriate study drugs for each planned study visit in opaque drug envelopes labeled with an identification number and visit information.

At the enrollment visit, research personnel interviewed pregnant women who expressed interest in the study about their socioeconomic status and obstetric history, provided them with pre-test HIV counseling, and performed an antenatal examination. The duration of pregnancy was determined by measuring the fetal biparietal diameter and femur length with an ultrasound. Hadlock tables were used to calculate fetal age. A laboratory assistant with extensive experience assessed all participants for blood hemoglobin (Hb) concentration, peripheral blood malaria parasitemia, and syphilis reactivity. HIV testing was offered to all enrolled participants but the testing was optional.

Eligible persons who consented to participate signed or thumb-printed an informed consent form and picked one envelope with an identification number. Each identification number was randomized to one of the three intervention groups. A research assistant not involved in outcome assessment gave the corresponding pre-packed study drugs to the participant under direct observation and monitored her for possible adverse reactions.

2.5 Follow-Up Scheme and Variable Descriptions

2.5.1 Mortality

Child mortality was assessed during the first 5 years of life. Information about child mortality was collected as soon as the study team heard about the death of the child or if the child did not show up for the scheduled study clinic visit for anthropometric measurements between 1 and 60 months of age. The study team traced the caretaker and collected mortality information if the child had died. Information on child mortality was collected using a structured verbal autopsy questionnaire administered to the mother or another primary caretaker of the child.

For this study, we defined miscarriage as non-induced loss of pregnancy before 22.0 completed gestation weeks and stillbirth as fetal death at or after 22.0 gestation weeks. Early neonatal death was defined as death of a live-born baby within 7 days of birth and late neonatal death was defined as death within 8–28 days of birth. Postneonatal death was defined as death between 29 days to 1 year of age and child death was defined as death between 1–5 years of age. Total number of deaths was calculated as the sum of miscarriages, stillbirths, neonatal deaths, and child deaths occurring between the time of enrollment and 5 years after delivery.

Perinatal mortality rate was defined as the number of stillbirths and early neonatal deaths (died within 7 days of delivery) divided by the total number of births at or after 22.0 gestational weeks. Neonatal mortality rate was defined as the number of deaths occurring within 28 days of delivery divided by the number of live births. Infant mortality rate was defined as the number of deaths occurring within 0–365 days of delivery divided by the number of live births, and under-5 mortality rate was defined as the number of deaths occurring between 0–5 years of age divided by the number of live births. We report perinatal, neonatal, infant, and under-5 mortality rates as the number of deaths per 1,000 births.

2.5.2 Morbidity

Child morbidity was measured as the number of NS visits made by the participant during the first 3 years of life. We recorded information on child morbidity in real time when the child made a NS visit to a health center. The number of NS visits was collected on structured data collection forms by the clinician doing the examination and did not include normal under-5 clinic visits. We used the number of NS visits as a proxy for morbidity because we did not have direct data on child morbidity.

We calculated the total number of NS visits to a health facility made by the participant during the first 3 years of life and during the first, second, and third year of life separately. We calculated the incidence of NS visits by dividing the number of NS visits by the number of months in the study during the first 3 years of life and during the first, second, and third year of life. We calculated time in follow-up as months with the following formula: 12 * (last day in study - date of birth) / 365.25. We calculated time in study during the first, second and third year of life with the formula: 12 * (last day in study during first/second/third year of life - first day in study during first/second/third year of life) / 365.25. We identified participants with the incidence of NS visits above the 75th and the 90th percentile.

2.5.3 Child Growth

Child growth was monitored by measuring length/height, weight, head circumference, and MUAC at the study clinic visit at the age of 3, 6, 9, 12, 15, 18, 24, 30, 36, 48, and 60 months. Anthropometrists measured child length (for children ≤ 24 months) with a kiddimetre (Raven Equipment Ltd; reading increment of 1 mm) or height (for children > 24 months) with a Harpenden stadiometre (Holtain Limited; reading increment of 1 mm).[1] Weight was normally measured with a SECA scale (SECA 834, Chasmors Ltd; reading increment of 10 g) or, at 36 months and beyond, was occasionally measured erroneously with a bathroom scale (reading increment of 1 kg). Head and arm circumference were measured with non-elastic plastic tape (Lasso-o tape, Harlow Printing Limited; reading increment of 1 mm). All measurements were recorded on a structured data collection form.

For anthropometric variables targeted to be measured before 24 months of age, we considered the data missing if the actual measurement date was off by ± 4 weeks from the target date. For variables targeted to be measured at or after 24 months of age, we considered the data missing if the actual measurement date was off by ± 8 weeks from the target date.

We calculated age- and sex-standardized anthropometric indices (height-for-age z-score [HAZ], weight-for-age z-score [WAZ], weight-for-height z-score [WHZ], head circumference-for-age z-score, MUAC-for-age z-score) by using World Health Organization (WHO) Child Growth Standards (WHO Multicentre Growth Reference Study Group 2006; de Onis et al. 2007). Only HAZ and WAZ could be derived for children measured between 60–62 months given that there is not a weight-for-height, head circumference,

[1] Although this study measured length for children ≤ 24 months, for simplicity and ease of reading, when referring to results for children ≤ 24 months, we use the terms weight-for-height z-score and height-for-age z-score rather than weight-for-length z-score and length-for-age z-score for this demographic group.

or MUAC WHO reference for children 60 months of age and older (de Onis et al. 2007). Values below -2 z-scores were considered indicative of stunting, underweight, wasting, small head circumference, and low MUAC. Values below -3 z-scores were considered indicative of severe stunting, severe underweight, severe wasting, very small head circumference, and very low MUAC. We also calculated deviation of individual length/height, weight, head circumference, and MUAC measurements from the corresponding WHO 2006 age- and sex-specific median reference.

2.5.4 Child Development

When the children were 60 months of age, a trained and certified research assistant assessed their development with Griffith's Mental Development Scales for children 2–8 years of age (Luiz et al. 2006).[2] Griffith's Mental Development Scales for children 2–8 years assesses six areas of development: locomotor skills, personal-social skills, language, eye and hand coordination, performance, and practical reasoning.

- Subscale A: Locomotor—assesses gross motor skills, including the ability to balance and to coordinate and control movements.
- Subscale B: Personal-Social—measures proficiency in the activities of daily living, level of independence, and interaction with other children.
- Subscale C: Language—assesses receptive and expressive language.
- Subscale D: Eye and Hand Coordination—focuses on fine motor skills, manual dexterity, and visual monitoring skills.
- Subscale E: Performance—considers visuospatial skills including speed of working and precision.
- Subscale F: Practical Reasoning—assesses the ability to solve practical problems, understanding of basic mathematical concepts, and understanding of moral issues.

There are 38 items in each subscale. For each domain, the questions are organized hierarchically, i.e., easiest tasks first, most difficult ones last. The items are color coded to identify which items are similar.

The Griffith's Mental Development Scales have been used for almost 40 years to assess children's development. The tool has been standardized in the United Kingdom and South Africa and does not have standardized norms for Malawi. In Western studies, some predictive validity of Griffith's scales has been shown in relation to IQ at 5 years of age (Bowen et al. 1996). In many of the landmark studies by Grantham-McGregor on malnutrition and developmental outcomes, Griffith's scales were used because it has reasonable stability over time, has clear standardized scoring systems, and good concurrent validity with the Stanford-Binet intelligence scale (Grantham-McGregor and Ani 2001).

In the LAIS trial, two trained research assistants directly administered the Griffith's scales to the children to assess their ability to perform tasks. If children were unable to do the task, a cross mark was placed in the box in the questionnaire. If they were able to do the task, a tick mark was placed in the box. We used all the questions in the assessment tool for children 2–8 years.

The target time point for the developmental assessment was at 60 months of age. As there were some delays in starting the assessments, the age at time of assessment for all but one participant ranged from 59 months to 74 months, with one participant falling outside that range and assessed at 48 months of age (25^{th} percentile 60 months of age, median 60 months of age, 75^{th} percentile 66 months of age). The distribution of age was skewed to the right though the number of children assessed between 60 and 74

[2] Griffith's scales for children 2–8 years of age is presented in Appendix 1.

months of age was distributed evenly across this age span. We did not exclude any participants from the analyses based on the age of assessment. To take differences in age at time of assessment into account, we adjusted all models for child age (Cheung 2014; McNamee 2005). Because the assessment tool has not been assessed for gender influence in the local culture, we also adjusted for child sex.

Normally, developmental scores on the Griffith's scales can be compared to reference studies by calculating mental age and developmental quotient for each child and comparing those against international references. Because some of the items in the assessment tool were considered not appropriate in Malawi[3] (e.g., copies 24+ letters; copies a diamond) mental age and developmental quotient were not used as our main outcomes. Instead, we calculated the sum of passed items for each child and used this as our main outcome. Earlier studies have shown that the sum of passed items and using mental age or developmental quotient as an outcome gives equivalent results when estimating an association or the effect of an intervention (Cheung et al. 2008; Phuka et al. 2012). This applies to subscales as well as the total scale.

2.6 Statistical Analysis

2.6.1 General Approach to Statistical Analysis

Statistical analyses were conducted with Stata 13.1 (StataCorp, College Station, United States) according to a pre-specified analysis plan.

We calculated percentages and risk ratios for mortality outcomes, the incidence of NS visits above the 75th and the 90th percentile, and the prevalence of various forms of malnutrition. We calculated hazard ratios for mortality and the incidence of various forms of malnutrition and incidence rate ratios for the total number of NS visits. For anthropometric indices and developmental scores we calculated group means and differences between groups. For the time-to-event analysis an event of malnutrition was deemed to have happened at the midpoint between the last age when the child was observed to be non-malnourished and the first age when the child was observed to be malnourished.

2.6.2 Details of Statistical Methods

2.6.2.1 General Analysis

We used log-binomial regression models to estimate risk ratios for binary end-points at a single time point and negative binomial regression adjusted for time in follow-up to estimate incidence rate ratios for the total number of NS visits. We used least squares regression to calculate differences in means for continuous outcomes, Cox regression to estimate hazard ratios for mortality outcomes, and competing-risks regression to estimate cumulative incidence of various forms of malnutrition under the competing risk of death.

For mortality, morbidity, and growth outcomes the main analyses were done without imputations for missing data. However, the main analysis for development was done with multiple imputed data. We had developmental data for 949 (83.7%) participants out of a possible 1,134 who were still alive at 5 years of age. For those that we had developmental data available, 21% of participants had a missing value for one developmental item and 10% had missing values for two or more items. We replaced missing values according to the assumption rule from the Griffith's test (Luiz et al. 2006). For each domain, the questions

[3] The items considered not locally applicable were given a cross mark and assigned a zero in the scoring, which meant they carried no impact in the association analysis.

are organized hierarchically, i.e., easiest tasks first, most difficult ones last. Normally all children were administered all items but in some cases items were missed and there was missing data in the subscale. If a child was able to complete seven consecutive tasks, the child was considered to also be able to complete all easier tasks. If a child was not able to complete seven consecutive tasks, the child was considered unable to complete any of the more demanding tasks. All missing values before seven consecutive passes were replaced as passed. All missing values after seven consecutive fails were replaced as failed. For missing values after replacing according to the Griffith's test rule, we used multiple imputation to impute the rest. Variables used to impute missing items were the maternal background variables presented in Table 1, child sex, household assets index, intervention group, all anthropometric measurements available for the child across all time points, all subscale scores in Griffith's test, and child age at the time of assessment. If the participant did not have all items assessed in the subscale, we used the observed number of passed items as the lower limit for imputing the right-censored variable. We also included interactions with intervention group and number of previous pregnancies, maternal malaria status at enrollment, HIV status, height, BMI at enrollment, gestational age at enrollment, maternal age, education, Hb at enrollment, and child sex in the imputation model. We did not include in the development analyses values for participants who had died before the age of 5 years.

Clustering of participants due to twin pregnancies was taken into account by using robust standard errors that allow for intragroup correlation (Yelland et al. 2015). To prevent inflated type I errors due to multiple testing, we began hypothesis testing with a global null hypothesis that the three groups were equivalent. Pairwise comparisons were carried out in any case but the interpretation of the results was that pairwise null hypotheses were rejected only if the global null hypothesis was also rejected (Cheung 2014). We used Wald's test to test the global null hypothesis of no differences between groups. We rejected the hypotheses of the three groups being equivalent if $p < 0.05$. For the developmental analysis we considered the comparison of differences in total score between the groups as the primary analysis of the study and, as such, it did not require multiplicity adjustment. Analyses with the six subscales were adjusted for multiplicity by using Holm's adjustment (Aickin and Gensler 1996), taking into account that there were six tests.[4] Raw p-values are presented in the tables (Tables 7b-7g) but interpretation of the results is based on Holm's adjusted p-values and these are the p-values presented in the text. We did not adjust the p-values for pairwise comparisons for multiplicity.

Except for developmental scores, where all models were adjusted for child sex and age at the time of developmental measurement, all main results are shown without covariate adjustments, but as a sensitivity analysis we also estimated coefficients adjusted for a set of covariates. Variables tested for inclusion in the models as covariates were: number of previous pregnancies, maternal malaria at enrollment, HIV status, height, BMI at enrollment, gestational age at enrollment, age, education, Hb at enrollment, and child sex. All regression models for the morbidity and mortality outcomes were adjusted for the same set of covariates based on whether the potential covariate was associated with any morbidity or mortality outcome at $p < 0.05$. All regression models for anthropometric outcomes were adjusted for the same set of covariates based on whether the potential covariate was associated with any anthropometric outcome at 24 months. Regression models for total developmental score were adjusted for covariates associated with total developmental score at $p < 0.05$. Because of the large sample size, we were not concerned about losing one degree of freedom for each covariate and loss of precision even

[4] In morbidity, mortality, and growth analyses we did not adjust for multiple comparisons because we considered different sets of hypotheses as independent families of hypotheses. Statistical adjustment for multiple comparisons in one family does not need to consider the other families. In the case of the development analyses, we analyzed the total developmental score and the subscale scores, which were used to calculate the total score so we considered them as the same family of hypotheses.

though we did not select covariates for each outcome separately and thus might be using some covariates that were not relevant for that specific outcome (Cheung 2014).

We performed the covariate selection with log-binomial regression for binary endpoints, negative binomial regression for counts, and least squares regression for continuous outcomes. To control for possible confounding, we put all variables into the model at once, except for maternal age and number of previous pregnancies, and those that showed a statistically significant association ($p < 0.05$) with any of the outcomes were included in the model as covariates. Because maternal age and number of previous pregnancies were strongly correlated with each other, we performed covariate selection in separate models using each variable at a time and in case both of them were indicated as covariates we created two adjusted models and chose the one with better goodness-of-fit (R^2 for least-square regression models, or Bayesian information criterion [BIC] for log-binomial and negative binomial regression models).

Anthropometric z-scores at 24 and 60 months of age were adjusted for the corresponding z-score value for the child at 1 month in order to test if this adjustment decreased the difference between groups at 24 and 60 months. If a decrease was observed, but there still remained a difference between groups, this would suggest that part of the difference observed at the later time point was due to the difference at 1 month and part was due to intervention effects accrued after 1 month. If differences between groups disappeared after adjustment for the 1 month z-score, this would suggest that any observed difference between intervention groups at the later time point was only due to the difference observed at 1 month. MUAC-for-age z-score was not included in this analysis because MUAC-for-age z-score cannot be calculated for children under 3 months of age (WHO Multicentre Growth Reference Study Group 2006).

As exploratory analyses, we also tested for the presence of an interaction between the intervention and pre-specified maternal and child characteristics by Wald's test. When testing for interaction effects, we included the main effect of each term and the interaction term in the model. We performed analyses stratified by the respective variables if the interaction term was significant at $p < 0.1$. The variables tested for interaction were the same as those tested for covariate selection: number of previous pregnancies, maternal malaria at enrollment, HIV status, height, BMI at enrollment, gestational age at enrollment, age, education, Hb at enrollment, and child sex. Only 5.0% of mothers had a BMI < 18.5 and 3.0% were less than 145 cm tall, so we stratified these variables at the median for interaction testing instead of using the conventional cut-off points of 18.5 for BMI and 145 cm for height. Median was used as a cut point for all other continuous variables as well, to ensure an adequate sample size across the interaction categories.

In the pre-specified analysis plan, we defined 24 months to be the main time point for anthropometric measurements and we used this time point for carrying out the interaction tests and applied these results to other time points as well. For mortality outcomes a total of 50 interaction tests were carried out, for morbidity outcomes a total of 40 tests for interaction were carried out, for growth outcomes a total of 120 tests for interaction were carried out, and for development a total of 10 tests for interaction were carried out.

The purpose of the interaction testing was exploratory rather than confirmatory. Because we were carrying out many interaction tests and applied a cut-off value of $p < 0.1$ to denote significance, we knew that many tests would be statistically significant due to pure chance. The cut-off of $p < 0.1$ was selected in order to be generous in detecting interactions even though some of them would be false positives. This has been taken into account in the interpretation of the results.

2.6.2.2 Sensitivity Analysis for Growth

At 3 years of age and beyond, some children were occasionally weighed with bathroom scales instead of SECA scales, in which case their weights were rounded to the nearest kilogram. This affected some weight measurements between 36 and 60 months of age and hence also affected individual weight-for-age and weight-for-height z-scores. Because no record was made of weight measurements that were taken with bathroom scales, it was not possible to identify participants with weight rounded to the nearest kilogram. As a sensitivity analysis, we considered all full kilogram weight measurements recorded at or after 36 months as censored within an interval of ± 0.5 kg of the full kilogram and used multiple imputation with interval censoring to replace the value. Variables used to impute weight measurements were the maternal background variables presented in Table 1, intervention group, and all anthropometric measurements available for the child across all time points. This imputation created one new dataset, which was used in the sensitivity analysis for weight measurements rounded to the nearest full kilogram. After imputation we ran the analysis on the full dataset with imputed values. Only unadjusted analyses were carried out with imputed weight measurements. Interaction terms were not tested.

As a second sensitivity analysis, we used multiple imputation to impute missing anthropometric values for those children lost to follow-up, as recommended by Little et al. (2012). We did not include in the analysis values for participants who had died before the time point of the analysis, e.g., mean HAZ at 24 months of age excluded participants who had died before 24 months of age. Variables used in the imputation model were the same as those used to impute weights measured at a full kilogram value. This imputation created a second new dataset, which was used in sensitivity analysis for imputations for missing anthropometric values. After imputation we ran the analysis on the full dataset with imputed values. Only unadjusted analyses were carried out with imputed data. Interaction terms were not tested.

2.6.2.3 Descriptive and Sensitivity Analyses for Development

We carried out an attenuation analysis of the effect of pregnancy outcomes on child development to see whether inclusion of covariates to the model would decrease the differences between groups. The aim of this exploratory analysis was to find out if the effect of the intervention was mediated through the pregnancy outcomes or whether there was an unknown pathway whereby the intervention would affect the developmental score. We adjusted the analyses separately for duration of pregnancy, birth weight, head circumference-for-age z-score at 1 month of age, HAZ at 1 month of age, length-for-gestational age, weight-for-gestational age, and head circumference-for-gestational age. Length, weight, and head circumference for gestational age were calculated according to INTERGROWTH-21st Newborn Size at Birth Charts[5] (Villar et al. 2014). If an attenuation of the between-group difference was observed after the inclusion of a covariate, this would suggest that the intervention effect was (partly) mediated through the covariate or items associated with it.

To validate the developmental measurements of our study, we tested whether the developmental scores behave as we would expect based on earlier knowledge. Earlier studies have shown that maternal education, socio-economic status, and child growth are associated with child development (Cheung et al. 2001; Ivanans 1975). We tested whether developmental scores from our study showed similar associations.

[5] Weight-for-gestational age and head circumference-for-gestational age were calculated based on measurements taken at birth. Because length was not measured at birth and the first measurement was done at 1 month of age, we assumed that HAZ at birth was the same as HAZ at 1 month of age. HAZ was then converted into length (cm) at birth using the WHO growth charts. After that, length at birth was converted to length-for-gestational age using the INTERGROWTH-21st Newborn Size at Birth Charts.

The individual and household factors hypothesized to affect child development were maternal years of schooling, number of people in the household, household asset index (Filmer and Pritchett 2001), duration of pregnancy, child HAZ, head circumference-for-age z-score at 1 month of age, and child HAZ and head circumference-for-age z-score at 5 years of age. We created several regression models with total score as the dependent variable and the intervention group, child sex and age at the time of assessment, and the variables listed above as independent variables. First we tested the association between total developmental score and the exploratory variables by including each explanatory variable in a model controlling for child sex and child age at the time of assessment but no other variables. Next we created a multiple variable regression model with total score as the dependent variable and the intervention group, child sex and child age at the time of assessment, and all of the variables listed above as independent variables. This was done to test the association of these variables to the total developmental score.

Out of participants who were alive at 5 years of age, 16.3% did not have developmental assessment done and 25.5% of participants who had the assessment done had at least one missing item in subscale scores. Because of missing data, the main analysis was done with imputed values for missing items as described in section 2.6.2.1. As a sensitivity analysis we analyzed the data without any imputations and compared the results to those with imputed values. For this analysis, we excluded children who had missing items in any subscale from the analyses.

3 Results

3.1 Characteristics of the Study Sample

Of the 3,358 pregnant women invited to participate in the study 1,320 (39.3%) were enrolled and randomized to one of the three intervention groups: 436 to the control group, 441 to the monthly SP group, and 443 to the AZI-SP group. The most common reasons for not being enrolled in the study were that the woman was not interested or refused after screening, the woman was not pregnant, or that gestational age was less than 14 weeks or more than 26 weeks (Figure 1). Enrolled and non-enrolled women were approximately the same age (25 and 26 years, respectively) and had the same number of previous pregnancies (2.3 and 2.5, respectively) (Luntamo et al. 2010). At enrollment the three intervention groups were comparable except for small differences in the proportion of primiparous women and prevalence of malaria parasitemia (Table 1). Despite the intention to exclude twin pregnancies, some twin pregnancies were missed at enrollment and mothers gave birth to three, two, and two pairs of twins in the control, monthly SP, and AZI-SP groups, respectively (Figure 1).

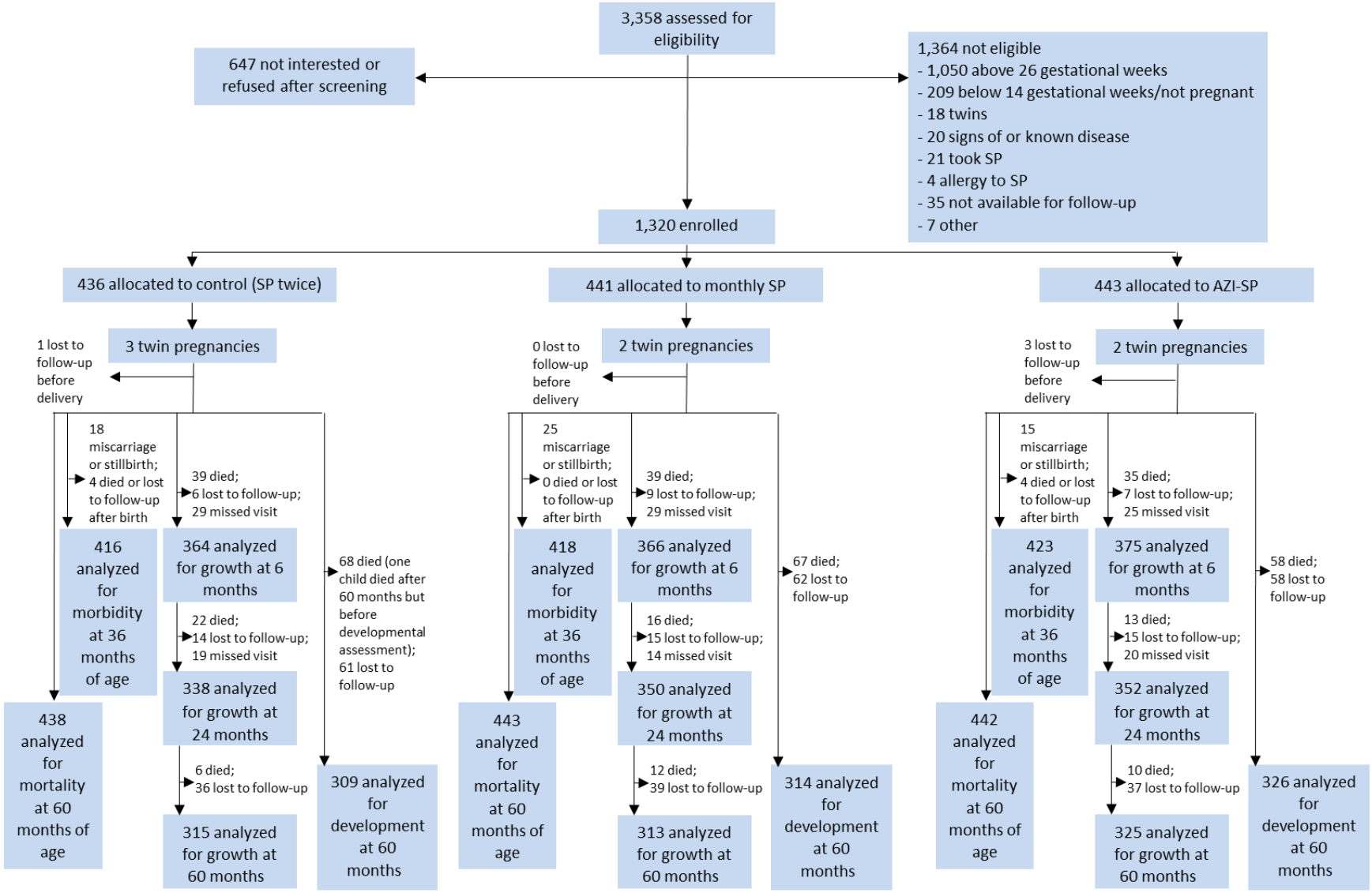
The mean (standard deviation [SD]) number of SP treatments received in the control, monthly SP, and AZI-SP groups were 2.0 (0.2), 4.0 (1.0), and 4.0 (0.9), respectively. The mean (SD) number of AZI doses received in the AZI-SP group was 2.0 (0.2) (Luntamo et al. 2010).

We obtained data on mortality at 5 years of age from 99.7% of participants and data on morbidity at 3 years of age from 94.7% of participants. We analyzed all participants, except for the four who were lost to follow-up before birth, for mortality outcomes (Figure 1). Growth data at 2 and 5 years of age was obtained from 78.2% and 71.8% of participants (Figure 1). Developmental data was obtained from 71.5% of participants (Figure 1). The success of follow-up was similar between the groups ($p = 0.896$ for morbidity at 3 years, $p = 0.660$ for growth at 2 years, $p = 0.733$ for growth at 5 years, and $p = 0.599$ for development at 5 years).

Table 1. Baseline Characteristics of Participating Women at Enrollment, by Study Group

Characteristic	Control (SP twice)	Monthly SP	AZI-SP
Number of enrolled women	436	441	443
Mean (SD) age, years	25 (7)	25 (7)	25 (6)
Mean (SD) height, cm	155.0 (5.5)	154.8 (5.4)	155.3 (5.6)
Mean (SD) BMI, kg/m²	21.7 (2.2)	21.8 (2.1)	21.9 (2.1)
Mean (SD) gestational age at enrollment, weeks	20.3 (3.0)	20.0 (3.2)	20.0 (3.0)
Proportion of primiparous	25.2% (110/436)	24.3% (107/441)	20.1% (89/443)
Proportion of HIV positive	12.1% (48/396)	16.0% (64/400)	12.3% (49/398)
Proportion of positive syphilis status	4.2% (18/433)	6.2% (27/435)	4.8% (21/440)
Mean (SD) blood Hb concentration, g/L	110 (19)	111 (17)	110 (20)
Proportion with moderate or severe anemia, Hb < 100 g/L	26.6% (116/436)	24.0% (106/441)	29.1% (129/443)
Proportion with severe anemia, Hb < 70 g/L	2.1% (9/436)	0.5% (2/441)	2.0% (9/443)
Proportion with microscopic peripheral blood malaria parasitemia	11.3% (49/435)	9.3% (41/441)	6.1% (27/443)
Proportion of literate participants	26.6% (116/436)	29.3% (129/441)	31.4% (139/443)
Mean (SD) years of schooling completed	2.1 (2.7)	2.2 (2.6)	2.4 (2.8)

Figure 1. Participant Flow of Mortality, Morbidity, Growth, and Developmental Analyses in CONSORT Recommended Format



3.2 Mortality

During the follow-up from enrollment to 5 years of age we recorded a total of 192 deaths. This included one miscarriage, 57 stillbirths, 76 deaths that occurred during the first year of life, and 58 deaths that occurred between 1 and 5 years of age. The proportion of children who died during the follow-up was 15.3% in the control group, 15.1% in the monthly SP group, and 13.1% in the AZI-SP group ($p = 0.603$) (Table 2, Figure 2). The number of deaths in the AZI-SP group compared to the other two groups was smaller for miscarriages and stillbirths, late neonatal deaths, and postneonatal deaths. The number of deaths was higher in the AZI-SP group than the other two groups during the early neonatal period, and the number of deaths was similar in all groups from 1 to 5 years of age. The difference in the number of deaths between groups was statistically significant only for the postneonatal period. Perinatal mortality rate, neonatal mortality rate, infant mortality rate, and under-5 mortality were 64/1,000, 25/1,000, 60/1,000, and 106/1,000, respectively, with no statistically significant difference between groups. Adjustment of the risk ratio estimates for maternal malaria, HIV status, height, BMI, Hb, and number of previous pregnancies at enrollment did not markedly change the results (details not shown).

Out of a total of 50 tests for interaction (five outcomes and 10 potential effect modifiers), without including covariates in the models, two (4%) gave statistically significant results ($p < 0.1$) (Appendix 2, Supplementary Table 1). We omitted late neonatal deaths from this analysis because there were only a total of four such deaths. Tests for interactions indicated that the number of previous pregnancies, maternal malaria at enrollment, maternal HIV status, duration of pregnancy at enrollment, maternal age, years of education, Hb at enrollment, and child sex did not modify the association between the intervention and mortality outcomes.

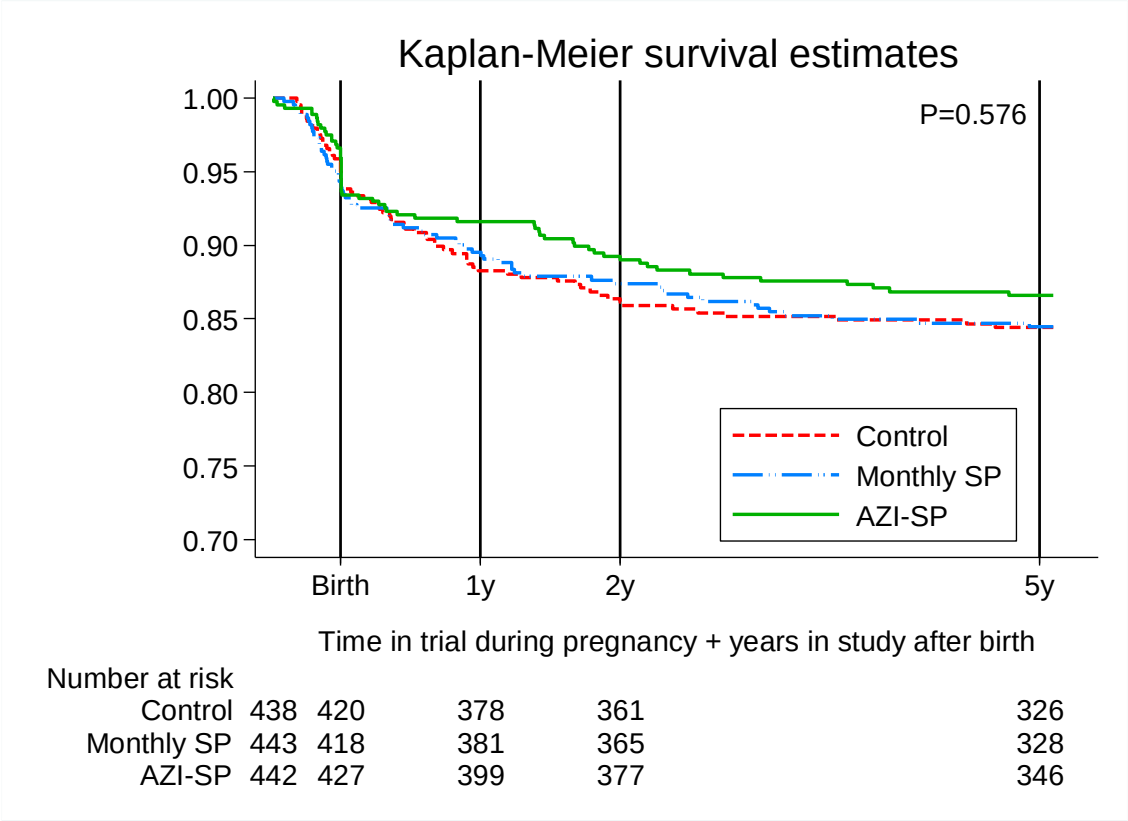
The association between the intervention and the proportion of early neonatal deaths was modified by maternal height ($p = 0.007$) (Table 3). Among children born to mothers whose height was above the median, the proportion of early neonatal deaths was 2.9% in the control group, 1.5% in the monthly SP group, and 1.3% in the AZI-SP group ($p = 0.451$). For infants born to mothers with height at or below the median, the proportion of early neonatal death was 1.4% in the control group, 0.5% in the monthly SP group, and 5.5% in the AZI-SP group ($p = 0.013$). The risk ratio in the AZI-SP group for early neonatal deaths was 3.89 ($p = 0.038$) compared to the control group and 11.99 ($p = 0.018$) compared to the monthly SP group.

The association between the intervention and the proportion of miscarriages and stillbirths was modified by maternal BMI ($p = 0.086$) (Table 3). Among mothers with a BMI above the median, the proportion of miscarriages and stillbirths was 3.9% in the control group, 7.5% in the monthly SP group, and 3.1% in the AZI-SP group ($p = 0.078$). Among mothers with a BMI at or below median, the proportion of miscarriages and stillbirths was almost the same in all groups (4.4% in the control group, 3.7% in the monthly SP group, and 3.7% in the AZI-SP group, $p = 0.921$).

Table 2. Number of Deaths by Intervention Group

Variable	Intervention groups				Comparison between the groups—risk ratio (95% confidence interval [CI])					
	Control (SP twice) *(n=438)*	Monthly SP *(n=443)*	AZI-SP *(n=442)*	Overall p-value	AZI-SP and control group	p-value	AZI-SP and monthly SP group	p-value	Monthly SP and control group	p-value
Proportion of children who died (miscarriage, stillbirth, death)	15.3% (67/438)	15.1% (67/443)	13.1% (58/442)	0.603	0.86 (0.62 to 1.19)	0.359	0.87 (0.62 to 1.20)	0.397	0.99 (0.72 to 1.35)	0.943
Proportion of miscarriages or stillbirths	4.1% (18/438)	5.6% (25/443)	3.4% (15/442)	0.253	0.83 (0.42 to 1.62)	0.577	0.60 (0.32 to 1.13)	0.112	1.37 (0.76 to 2.48)	0.293
Proportion of early neonatal deaths (0–7 days)	2.1% (9/420)	1.0% (4/418)	3.3% (14/427)	0.093	1.53 (0.66 to 3.57)	0.326	3.42 (1.12 to 10.49)	0.031	0.45 (0.14 to 1.44)	0.177
Proportion of late neonatal deaths (8–28 days)	0.2% (1/420)	0.7% (3/418)	0.0% (0/427)	0.339	NA	NA	NA	NA	3.01 (0.31 to 28.90)	0.339
Proportion of postneonatal deaths (29 days–1 year)	5.5% (23/420)	3.3% (14/418)	1.9% (8/427)	0.023	0.34 (0.15 to 0.76)	0.008	0.56 (0.24 to 1.32)	0.185	0.61 (0.32 to 1.17)	0.139
Proportion of child deaths (1–5 years)	3.8% (16/420)	5.0% (21/418)	4.9% (21/427)	0.651	1.29 (0.68 to 2.44)	0.432	0.98 (0.54 to 1.76)	0.944	1.32 (0.70 to 2.49)	0.394
Perinatal mortality rate (stillbirth, death 0–7 days)	62/1,000	66/1,000	64/1,000	0.973	1.03 (0.61 to 1.73)	0.911	0.97 (0.58 to 1.62)	0.907	1.06 (0.64 to 1.76)	0.816
Neonatal mortality rate (0–28 days)	24/1,000	17/1,000	33/1,000	0.349	1.38 (0.61 to 3.13)	0.446	1.96 (0.78 to 4.9)	0.151	0.7 (0.27 to 1.83)	0.471
Infant mortality rate (0–365 days)	79/1,000	50/1,000	52/1,000	0.156	0.66 (0.38 to 1.12)	0.122	1.03 (0.57 to 1.86)	0.934	0.64 (0.38 to 1.09)	0.098
Under-5 mortality rate (0–5 years)	117/1,000	101/1,000	101/1,000	0.683	0.86 (0.58 to 1.28)	0.461	1.00 (0.67 to 1.51)	0.991	0.86 (0.58 to 1.27)	0.452

Figure 2. Mortality Survival Curve by Intervention Group, from Enrollment to 5 Years of Age



Time zero in time-to-event analysis is the time of enrollment. Time to death during pregnancy was the time between enrollment and miscarriage/stillbirth. All pregnancies resulting in live birth were coded to have lasted 25 weeks and time in study after birth was added to that.[6]

[6] All stilbirths happened before the woman had been in the study for 25 weeks. If the pregnancy resulted in miscarriage/stillbirth, time in study was the time between enrollment and miscarriage/stillbirth. If the pregnancy resulted in live birth, time in study was set to 25 weeks to set the starting point of time in study after birth to be the same for all children, i.e., if the child was stillborn at week 13 of the study, time in study was 13 weeks; if the child was born alive at week 20 of the study and died at 12 months, time in study was 25 weeks during pregnancy + 12 months after pregnancy; and if the child was born at week 27 of the study and died at 12 months, time in study was 25 weeks during pregnancy + 12 months after pregnancy.

Table 3. Proportion of Miscarriages and Stillbirths and Early Neonatal Deaths by Intervention Group, Stratified by Maternal BMI and Height

Variable	Intervention groups					Comparison between the groups—risk ratio (95% CI)					
	Interaction test p-value	Control	Monthly SP	AZI-SP	Overall p-value	AZI-SP and control group	P-value	AZI-SP and monthly SP group	P-value	Monthly SP and control group	P-value
Maternal height above median: Proportion of early neonatal deaths	0.007	2.9% (6/209)	1.5% (3/201)	1.3% (3/227)	0.451	0.46 (0.12 to 1.81)	0.267	0.89 (0.18 to 4.33)	0.881	0.52 (0.13 to 2.05)	0.351
Maternal height at or below median: Proportion of early neonatal deaths		1.4% (3/211)	0.5% (1/217)	5.5% (11/199)	0.013	3.89 (1.08 to 14.06)	0.038	11.99 (1.54 to 93.51)	0.018	0.32 (0.03 to 3.10)	0.328
Maternal BMI above median: Proportion of miscarriages and stillbirth deaths	0.086	3.9% (8/208)	7.5% (17/227)	3.1% (7/225)	0.078	0.81 (0.30 to 2.19)	0.676	0.42 (0.16 to 0.98)	0.046	1.95 (0.86 to 4.41)	0.110
Maternal BMI at or below median: Proportion of miscarriages and stillbirth deaths		4.4% (10/230)	3.7% (8/216)	3.7% (8/216)	0.921	0.85 (0.34 to 2.12)	0.730	1.00 (0.38 to 2.62)	1.000	0.85 (0.34 to 2.12)	0.730

3.3 Morbidity

We recorded a total of 5,162 NS visits during the first three years of life. Total time in follow-up was 3,401 years. The incidence of NS visits per month was 0.12 in the control and monthly SP groups, and 0.13 in the AZI-SP group (p = 0.710) (Table 4). There were no differences between groups in the incidence of NS visits during the first, second, or third year of life. The proportion of participants with an incidence of NS visits above the 75th percentile during the 3-year follow-up was 19.2%, 22.7%, and 19.9% (p = 0.408) for the control, monthly SP, and AZI-SP groups. The proportion with an incidence of NS visits above the 90th percentile were 10.3%, 10.5%, and 9.0% (p = 0.719), respectively. Adjustment of the NS visit analyses for maternal malaria, HIV status, height, BMI, Hb, and number of previous pregnancies at enrollment did not change the results (details not shown).

Out of 40 tests for interaction carried out with morbidity outcomes, without including covariates in the models, five (12.5%) showed statistical significance (p < 0.1) (Appendix 2, Supplementary Table 2). However, there were no consistent patterns in the results of the interaction tests or in the subgroup analyses (Appendix 2, Supplementary Table 3).

Table 4. Incidence of Non-Scheduled Visits by Intervention Group during the First 3 Years of Life and during the First, Second, and Third Year of Life

Variable	Incidence				Comparison between the groups—incidence rate ratio (95% CI)					
	Control *(n=416)*	Monthly SP *(n=418)*	AZI-SP *(n=423)*	Overall p-value	AZI-SP and control group	P-value	AZI-SP and monthly SP group	P-value	Monthly SP and control group	P-value
Time in follow-up during first 3 years (months)	13,400	13,496	13,913							
Incidence (number) of NS visits[1] during first 3 years of life	0.12 (1,671)	0.12 (1,661)	0.13 (1,830)	0.710	1.02 (0.90 to 1.16)	0.712	1.05 (0.93 to 1.20)	0.408	0.97 (0.85 to 1.11)	0.668
Time in follow-up during first year of life (months)	4,737	4,757	4,844							
Incidence (number) of NS visits[1] during first year of life	0.25 (1,192)	0.24 (1,160)	0.26 (1,276)	0.455	1.05 (0.93 to 1.18)	0.463	1.08 (0.96 to 1.23)	0.216	0.97 (0.85 to 1.1)	0.616
Time in follow-up during second year of life (months)	4,413	4,434	4,624							
Incidence (number) of NS visits[1] during second year of life	0.08 (363)	0.08 (366)	0.08 (385)	0.994	1.01 (0.81 to 1.26)	0.929	1.01 (0.81 to 1.25)	0.926	1.00 (0.8 to 1.25)	0.997
Time in follow-up during third year of life (months)	4,250	4,304	4,445							
Incidence (number) of NS visits[1] during third year of life	0.03 (116)	0.03 (135)	0.04 (169)	0.087	1.41 (1.04 to 1.93)	0.029	1.22 (0.9 to 1.65)	0.192	1.16 (0.84 to 1.6)	0.365

[1] Incidence = number of events / total follow-up months

3.4 Growth

3.4.1 Continuous Outcomes

The mean (SD) HAZ of children in the study cohort was -1.38 (1.22) at 6 months, -2.11 (1.05) at 24 months, and -1.68 (0.94) at 60 months of age. The pattern of HAZ was similar in all intervention groups: HAZ decreased until the age of 24 months and increased thereafter up to 60 months (Figure 3, panel A). The mean HAZ was higher in the AZI-SP group than in the control or monthly SP groups at all time points. The difference in HAZ between the AZI-SP and the control group was 0.25 z-scores at 6 and 12 months, 0.17 z-scores at 24 months, 0.13 z-scores at 36 months, and 0.15 z-scores at 48 and 60 months (Table 5). Differences between groups were statistically significant at 6 ($p = 0.006$ AZI-SP vs. control) and 12 ($p = 0.004$ AZI-SP vs. control) months of age but not thereafter.

The mean (SD) absolute length/height of children in the study cohort was 63.8 (2.8) cm at 6 months, 80.6 (3.3) cm at 24 months, and 101.9 (4.4) cm at 60 months. The mean difference in length/height between groups fluctuated very little between 6 and 60 months (Figure 4). For instance, the difference between the AZI-SP and the control group varied from 0.4 cm to 0.7 cm between 1 month and 60 months.

All three groups were similar in terms of the pattern shown for each z-score. The pattern of WAZ was similar to that of HAZ with a decrease until 24 months, but unlike HAZ, WAZ plateaued after 24 months (Figure 3, panel B). WHZ decreased rapidly between 1 and 12 months and continued to decrease after 12 months, but more slowly (Figure 3, panel C). Head circumference-for-age z-score and MUAC-for-age z-score showed a continual decrease from 1 to 60 months (Figure 3, panels D and E, respectively).

The AZI-SP group had a higher mean WAZ and head circumference-for-age z-score compared to the control and monthly SP groups at all time points (Figure 3, panels B and D). The differences in WAZ and head circumference-for-age z-score between the AZI-SP group and the control and monthly SP groups were statistically significant at 6 months but not thereafter (Table 5). Differences between groups in mean WHZ were not consistently in favor of AZI-SP or any other intervention group over time and there were no statistically significant differences at any time point (Table 5 and Figure 3, panel C). For MUAC-for-age z-score AZI-SP was higher compared to the control from 6 to 36 months of age but at 48 and 60 months those differences had disappeared (Figure 3, panel E). The difference in MUAC-for-age z-score between the AZI-SP and the control group was statistically significant at 6 months ($p = 0.016$) but not thereafter (Table 5).

The mean (SD) absolute weight of children in the study cohort was 7.1 (1.0) kg at 6 months, 10.3 (1.3) kg at 24 months, and 15.4 (1.7) kg at 60 months. The mean (SD) head circumference was 43.1 (1.5) cm at 6 months, 47.4 (1.5) cm at 24 months, and 49.4 (1.5) cm at 60 months. The mean (SD) MUAC at the respective time points was 13.4 (1.2) cm, 14.2 (1.1) cm, and 15.2 (1.0) cm. Mean weight was 74–232 g higher in the AZI-SP group compared to the control group throughout the follow-up. The difference was statistically significant at 6 months (190 g, $p = 0.007$, AZI-SP vs. control). Absolute head circumference and MUAC in the AZI-SP group were equal to or slightly higher than the control group throughout the follow-up with no statistically significant difference at any time point (details not shown).

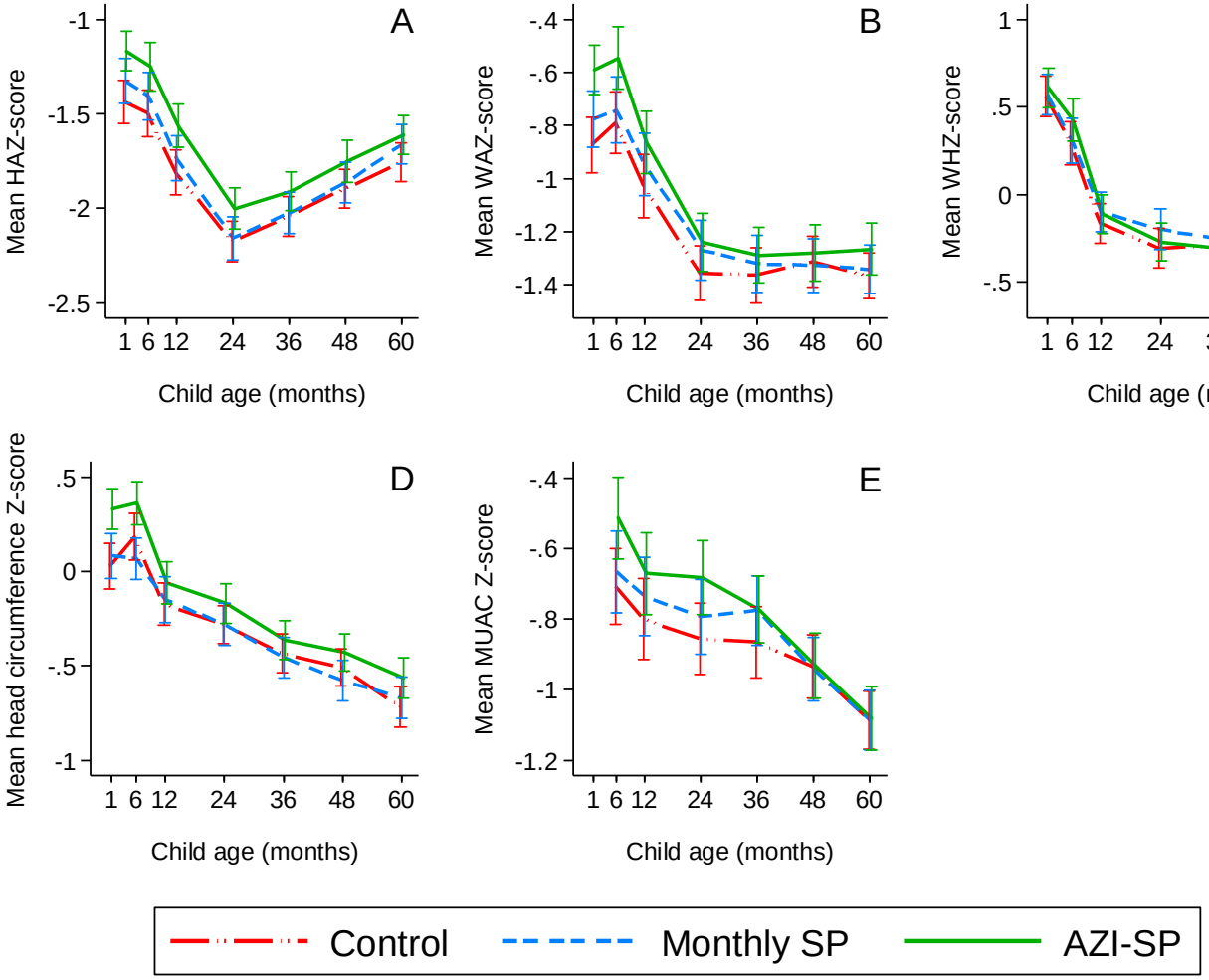
When adjusted for HAZ at 1 month, the difference in mean HAZ between the AZI-SP group and the control group decreased from 0.17 to 0.07 at 24 months and from 0.15 to 0.05 at 60 months. The effect was similar when WAZ and head circumference-for-age z-score at 24 and 60 months were adjusted for the respective z-score value at 1 month. The difference in mean WAZ between the AZI-SP and the control group decreased from 0.11 to 0.01 at 24 months and from 0.10 to 0.02 at 60 months. The difference between the AZI-SP and the control group at respective time points decreased from 0.11 to

0.01 and 0.15 to 0.03 in mean head circumference-for-age z-score. The difference between AZI-SP and the control group in WHZ at 24 and 60 months remained the same after the adjustment for WHZ at 1 month (at 24 months with and without adjustment 0.04, at 60 months 0.02 without adjustment and 0.03 with adjustment) (details not shown).

Participants in the study population were on average 2.6 cm shorter at 1 month than in the WHO reference population. The mean difference in absolute length/height (cm) compared to the WHO reference population increased in all groups up to 36 months and stabilized after that (Figure 5, panel A). At 60 months, the mean deficit in absolute height in the study population compared to the WHO reference population was 7.9 cm.

Participants in the study population were on average 0.4 kg lighter at 1 month than the children in the WHO reference population and had on average a head circumference 0.2 cm above that of the reference population. There is no WHO age- and sex-specific reference value for MUAC measured less than 91 days of age, but at 6 months MUAC was on average 0.6 cm less in the study population than in the WHO reference population. Differences in absolute weight (kg), head circumference (cm), and MUAC (cm) compared to the WHO reference population increased over time in all groups (Figure 5, panels B, C, and D). At 60 months of age, the mean deficit in weight, head-circumference, and MUAC was 2.9 kg, 0.9 cm, and 1.5 cm.

Figure 3. Mean HAZ, WAZ, WHZ, Head Circumference-for-Age Z-Scores, and MUAC-for-Age Z-Scores



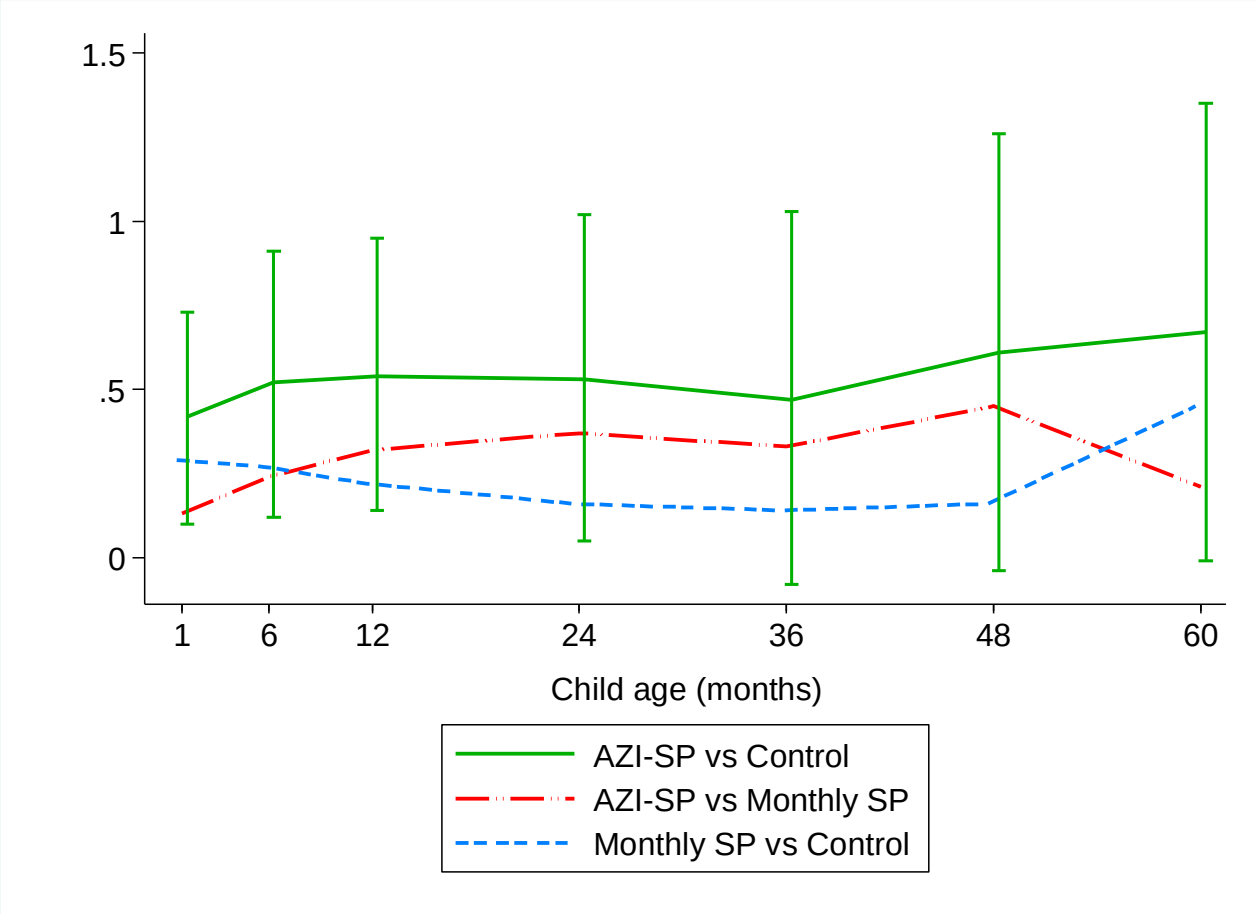
Mean HAZ (panel A), WAZ (panel B), WHZ (panel C), head circumference-for-age z-scores (panel D), and MUAC-for-age z-scores (E) at 1, 6, 12, 24, 36, 48, and 60 months of age by intervention group.

Table 5. Continuous Growth Outcomes by Intervention Group at 6, 12, 24, 36, 48, and 60 Months of Age

Outcome	Age	Mean (SD)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
		Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value
Mean (SD) height-for-age z-score (HAZ)	6 mo	-1.50 (1.18)	-1.40 (1.21)	-1.25 (1.25)	0.022	0.25 (0.07 to 0.43)	0.006	0.16 (-0.02 to 0.34)	0.087	0.09 (-0.08 to 0.27)	0.307
	12 mo	-1.81 (1.14)	-1.74 (1.13)	-1.56 (1.11)	0.011	0.25 (0.08 to 0.41)	0.004	0.17 (0.01 to 0.34)	0.039	0.07 (-0.10 to 0.24)	0.397
	24 mo	-2.17 (1.01)	-2.16 (1.08)	-2.00 (1.05)	0.055	0.17 (0.02 to 0.33)	0.028	0.16 (0.00 to 0.31)	0.053	0.02 (-0.14 to 0.17)	0.838
	36 mo	-2.04 (0.97)	-2.02 (1.02)	-1.91 (0.98)	0.163	0.13 (-0.02 to 0.28)	0.080	0.11 (-0.04 to 0.26)	0.137	0.02 (-0.14 to 0.17)	0.822
	48 mo	-1.90 (0.95)	-1.86 (0.99)	-1.75 (1.03)	0.148	0.15 (-0.01 to 0.30)	0.061	0.11 (-0.04 to 0.27)	0.147	0.03 (-0.12 to 0.18)	0.680
	60 mo	-1.76 (0.92)	-1.66 (0.94)	-1.61 (0.94)	0.140	0.15 (0.00 to 0.29)	0.050	0.05 (-0.10 to 0.20)	0.498	0.09 (-0.05 to 0.24)	0.208
Mean (SD) weight-for-age z-score (WAZ)	6 mo	-0.79 (1.13)	-0.74 (1.21)	-0.55 (1.15)	0.010	0.24 (0.08 to 0.41)	0.004	0.20 (0.03 to 0.37)	0.025	0.05 (-0.12 to 0.22)	0.597
	12 mo	-1.03 (1.12)	-0.95 (1.12)	-0.86 (1.14)	0.154	0.16 (0.00 to 0.33)	0.053	0.08 (-0.08 to 0.25)	0.328	0.08 (-0.09 to 0.25)	0.342
	24 mo	-1.36 (0.96)	-1.27 (1.07)	-1.24 (1.03)	0.295	0.11 (-0.04 to 0.26)	0.136	0.03 (-0.13 to 0.19)	0.727	0.09 (-0.07 to 0.24)	0.272
	36 mo	-1.36 (0.96)	-1.32 (1.00)	-1.29 (0.99)	0.614	0.08 (-0.07 to 0.22)	0.325	0.03 (-0.12 to 0.18)	0.676	0.04 (-0.11 to 0.20)	0.577
	48 mo	-1.31 (0.89)	-1.33 (0.93)	-1.28 (0.98)	0.816	0.03 (-0.11 to 0.18)	0.649	0.05 (-0.10 to 0.19)	0.535	-0.01 (-0.15 to 0.13)	0.860
	60 mo	-1.37 (0.78)	-1.34 (0.82)	-1.27 (0.89)	0.304	0.10 (-0.03 to 0.23)	0.132	0.08 (-0.06 to 0.21)	0.271	0.03 (-0.10 to 0.15)	0.699
Mean (SD) weight-for-height z-score (WHZ)	6 mo	0.29 (1.18)	0.31 (1.23)	0.43 (1.19)	0.246	0.14 (-0.04 to 0.31)	0.124	0.12 (-0.06 to 0.29)	0.185	0.02 (-0.16 to 0.19)	0.856
	12 mo	-0.16 (1.06)	-0.10 (1.08)	-0.11 (1.08)	0.711	0.05 (-0.11 to 0.21)	0.540	-0.01 (-0.17 to 0.14)	0.856	0.06 (-0.10 to 0.22)	0.431
	24 mo	-0.31 (1.05)	-0.20 (1.09)	-0.27 (1.02)	0.405	0.04 (-0.12 to 0.19)	0.659	-0.07 (-0.23 to 0.08)	0.361	0.11 (-0.05 to 0.27)	0.187
	36 mo	-0.29 (1.12)	-0.25 (1.07)	-0.31 (1.01)	0.787	-0.02 (-0.18 to 0.15)	0.833	-0.05 (-0.21 to 0.10)	0.493	0.04 (-0.13 to 0.21)	0.668
	48 mo	-0.27 (1.13)	-0.31 (1.15)	-0.34 (1.10)	0.707	-0.07 (-0.24 to 0.10)	0.410	-0.02 (-0.20 to 0.15)	0.778	-0.05 (-0.22 to 0.13)	0.599
	60 mo	-0.45 (1.03)	-0.5 (1.03)	-0.43 (1.02)	0.682	0.02 (-0.14 to 0.18)	0.835	0.07 (-0.09 to 0.23)	0.398	-0.05 (-0.22 to 0.11)	0.531

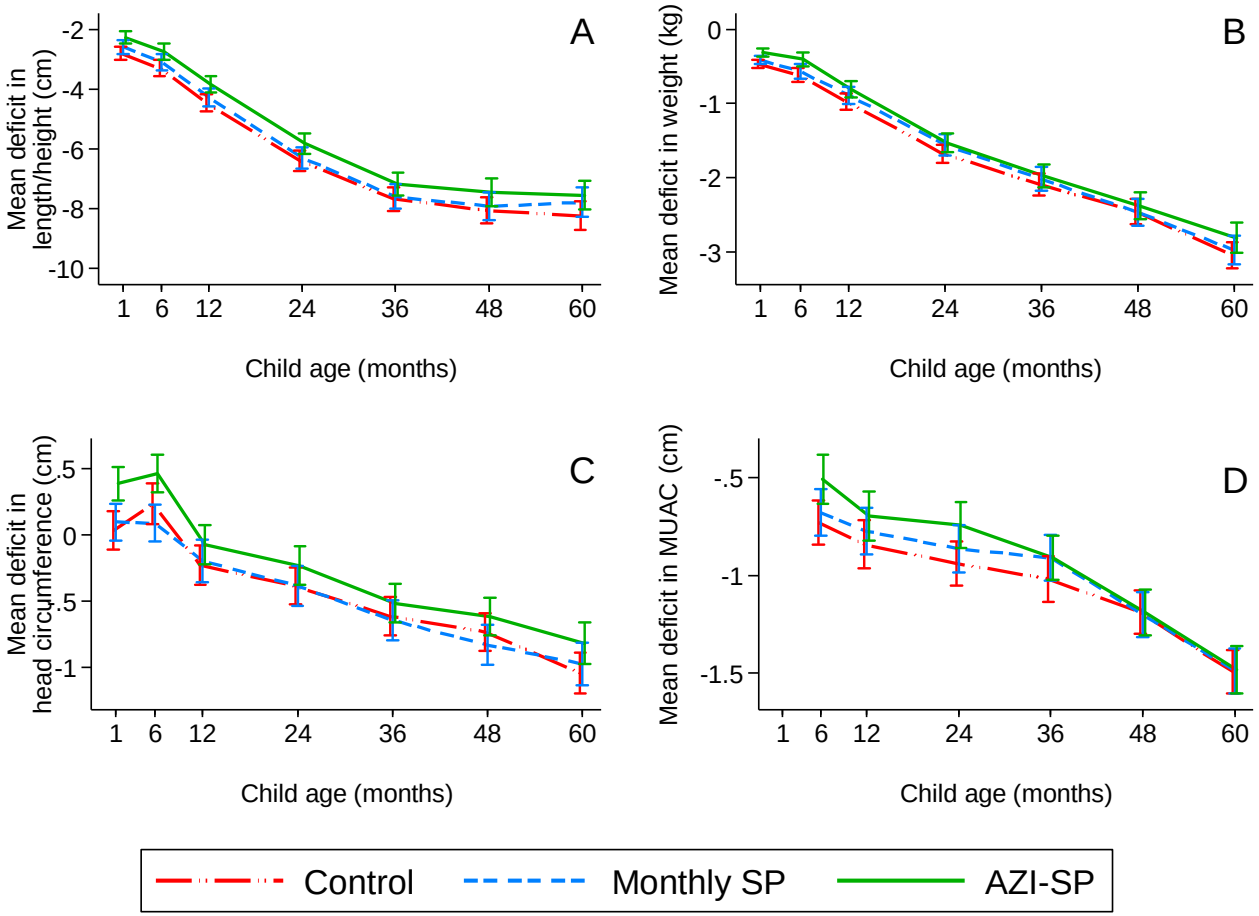
Outcome	Age	Mean (SD)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
		Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value
Mean (SD) head circumference-for-age z-score	6 mo	0.18 (1.20)	0.07 (1.07)	0.36 (1.12)	0.001	0.18 (0.01 to 0.35)	0.037	0.29 (0.13 to 0.45)	0.000	-0.11 (-0.28 to 0.05)	0.178
	12 mo	-0.17 (1.05)	-0.15 (1.15)	-0.06 (1.08)	0.334	0.11 (-0.04 to 0.27)	0.158	0.09 (-0.08 to 0.25)	0.287	0.02 (-0.14 to 0.19)	0.775
	24 mo	-0.28 (0.95)	-0.28 (1.05)	-0.17 (1.01)	0.241	0.11 (-0.03 to 0.26)	0.133	0.11 (-0.04 to 0.26)	0.158	0.00 (-0.15 to 0.15)	0.988
	36 mo	-0.43 (0.93)	-0.46 (1.00)	-0.37 (0.98)	0.450	0.07 (-0.07 to 0.21)	0.349	0.09 (-0.06 to 0.24)	0.231	-0.02 (-0.17 to 0.13)	0.770
	48 mo	-0.51 (0.91)	-0.58 (0.97)	-0.43 (0.90)	0.125	0.08 (-0.06 to 0.22)	0.260	0.15 (0.01 to 0.29)	0.042	-0.07 (-0.21 to 0.08)	0.346
	60 mo	-0.72 (0.95)	-0.67 (0.98)	-0.56 (0.98)	0.121	0.15 (0.00 to 0.31)	0.044	0.11 (-0.05 to 0.26)	0.173	0.05 (-0.11 to 0.2)	0.542
Mean (SD) MUAC-for-age z-score	6 mo	-0.71 (1.04)	-0.67 (1.12)	-0.51 (1.14)	0.044	0.19 (0.04 to 0.35)	0.016	0.15 (-0.01 to 0.32)	0.068	0.04 (-0.12 to 0.20)	0.606
	12 mo	-0.80 (1.08)	-0.74 (1.06)	-0.67 (1.12)	0.300	0.13 (-0.03 to 0.29)	0.121	0.07 (-0.09 to 0.23)	0.422	0.06 (-0.10 to 0.22)	0.440
	24 mo	-0.86 (0.95)	-0.79 (1.01)	-0.68 (1.00)	0.064	0.17 (0.03 to 0.32)	0.020	0.11 (-0.04 to 0.26)	0.147	0.06 (-0.09 to 0.21)	0.407
	36 mo	-0.87 (0.93)	-0.78 (0.91)	-0.77 (0.91)	0.344	0.09 (-0.05 to 0.23)	0.190	0.00 (-0.13 to 0.14)	0.961	0.09 (-0.05 to 0.23)	0.214
	48 mo	-0.93 (0.82)	-0.94 (0.83)	-0.93 (0.85)	0.987	0.00 (-0.13 to 0.13)	0.967	0.01 (-0.12 to 0.14)	0.875	-0.01 (-0.13 to 0.12)	0.907
	60 mo	-1.09 (0.74)	-1.09 (0.76)	-1.08 (0.83)	0.997	0.00 (-0.12 to 0.13)	0.940	0.00 (-0.12 to 0.13)	0.948	0.00 (-0.12 to 0.12)	0.992

Figure 4. Differences between Groups and 95% CI for AZI-SP versus Control in Length/Height



Differences between groups and 95% CI for AZI-SP vs. control in length/height (cm) at 1, 6, 12, 24, 36, 48, and 60 months of age by intervention group.

Figure 5. Difference in Absolute Length/Height, Weight, Head Circumference, and MUAC



Difference in absolute length/height (cm) (panel A), weight (kg) (panel B), head circumference (cm) (panel C), and MUAC (cm) (panel D) compared to WHO reference at 1, 6, 12, 24, 36, 48, and 60 months of age by intervention group.

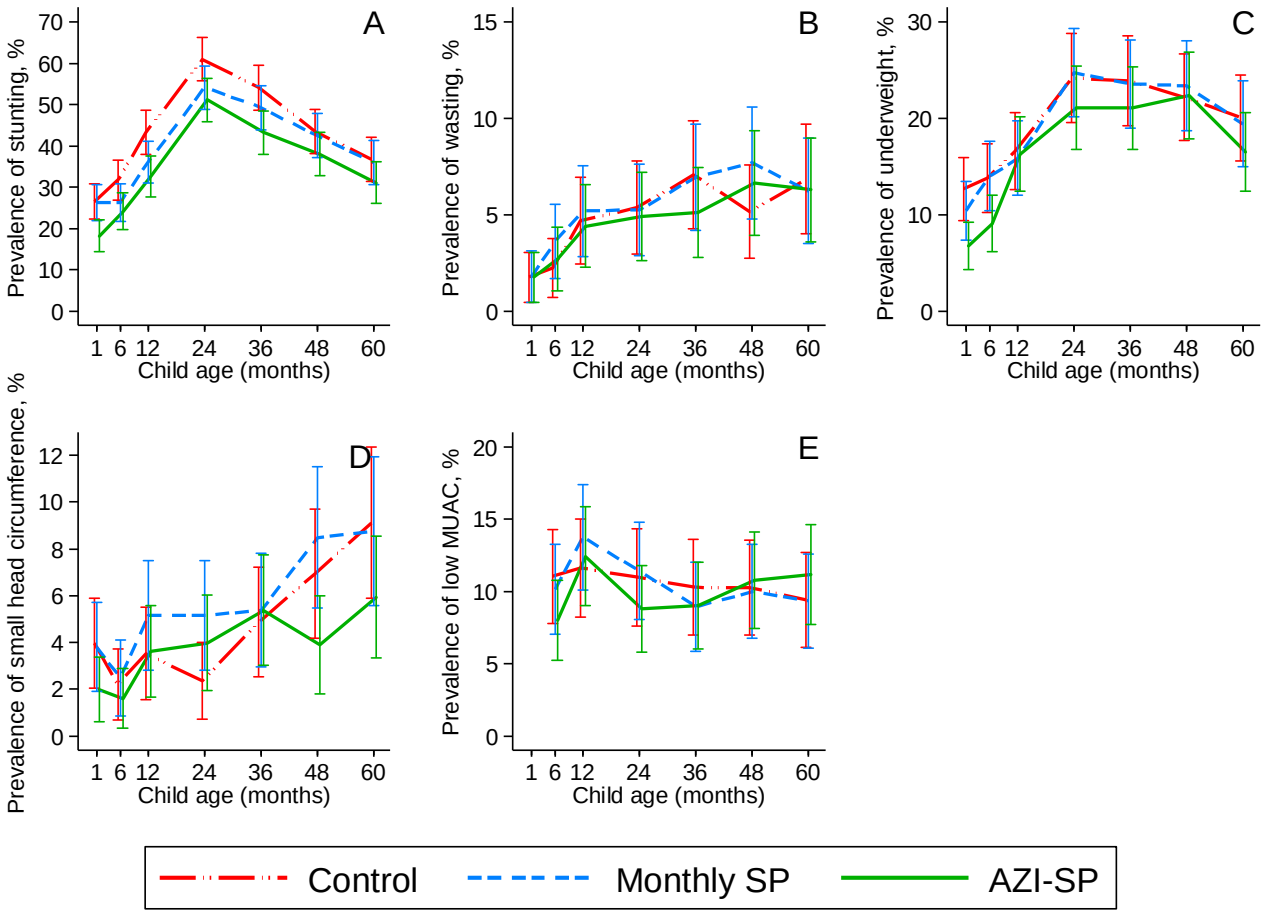
3.4.2 Prevalence and Incidence of Various Forms of Malnutrition

The prevalence of stunting varied between 27.4% (at 6 months) and 55.3% (at 24 months), and the prevalence of severe stunting varied between 7.5% (at 60 months) and 18.3% (at 24 months). The prevalence of stunting increased up to 24 months and decreased thereafter in all intervention groups (Figure 6, panel A). Compared to the control group, the prevalence of stunting for the AZI-SP group was 6–11 percentage points lower throughout the follow-up period. From 6 to 60 months, the risk ratio of stunting for the AZI-SP group compared to the control group varied between 0.75–0.87 (Table 6). Differences in the prevalence of stunting between the AZI-SP group and the control group were statistically significant at 12 months ($p = 0.004$), 24 months ($p = 0.010$), and 36 months ($p = 0.005$). The risk ratio of severe stunting was 0.73–0.93 for the AZI-SP group compared to the control group throughout the follow-up but the differences were not statistically significant.

The prevalence of other forms of malnutrition was lower than the prevalence of stunting throughout the follow-up (Figure 6). The prevalence of wasting increased until the age of 60 months (Figure 6, panel B). The prevalence of underweight increased up to age of 24 months in all groups and remained almost constant thereafter (Figure 6, panel C). The prevalence of small head circumference increased slightly from 1 month to 60 months (Figure 6, panel D). The prevalence of low MUAC remained almost constant from 6 to 60 months (Figure 6, panel E). Although the prevalence of wasting, underweight, and small head circumference was mostly lower in the AZI-SP group than the other two groups, none of the differences were statistically significant (Table 6; Figure 6, panels B–D). There were no differences between groups in prevalence of low MUAC at any time point (Table 6; Figure 6, panel E).

The cumulative incidence of stunting and severe stunting with competing risk of death by 60 months was significantly lower in the AZI-SP group compared to the other two groups (stunting: $p < 0.001$ AZI-SP vs. control, $p = 0.001$ AZI-SP vs. monthly SP; severe stunting: $p < 0.001$ AZI-SP vs. control, $p = 0.007$ AZI-SP vs. monthly SP) (Figure 7, panel A–B). Also, the cumulative incidence of underweight, small head circumference, and low MUAC were lower in the AZI-SP group than in the other two intervention groups by 5 years of age (Figure 7, panel C, E–F). The difference in the incidence of underweight between the AZI-SP and the control group was statistically significant ($p = 0.002$), whereas the differences with small head circumferences and low MUAC were not. There were no differences between groups in the incidence of wasting (Figure 7, panel D).

Figure 6. Prevalence and 95% of Confidence Interval



Prevalence and 95% CI of stunting (panel A), wasting (panel B), underweight (panel C), small head circumference (panel D), and low MUAC (panel E) at 1, 6, 12, 24, 36, 48, and 60 months of age by intervention group.

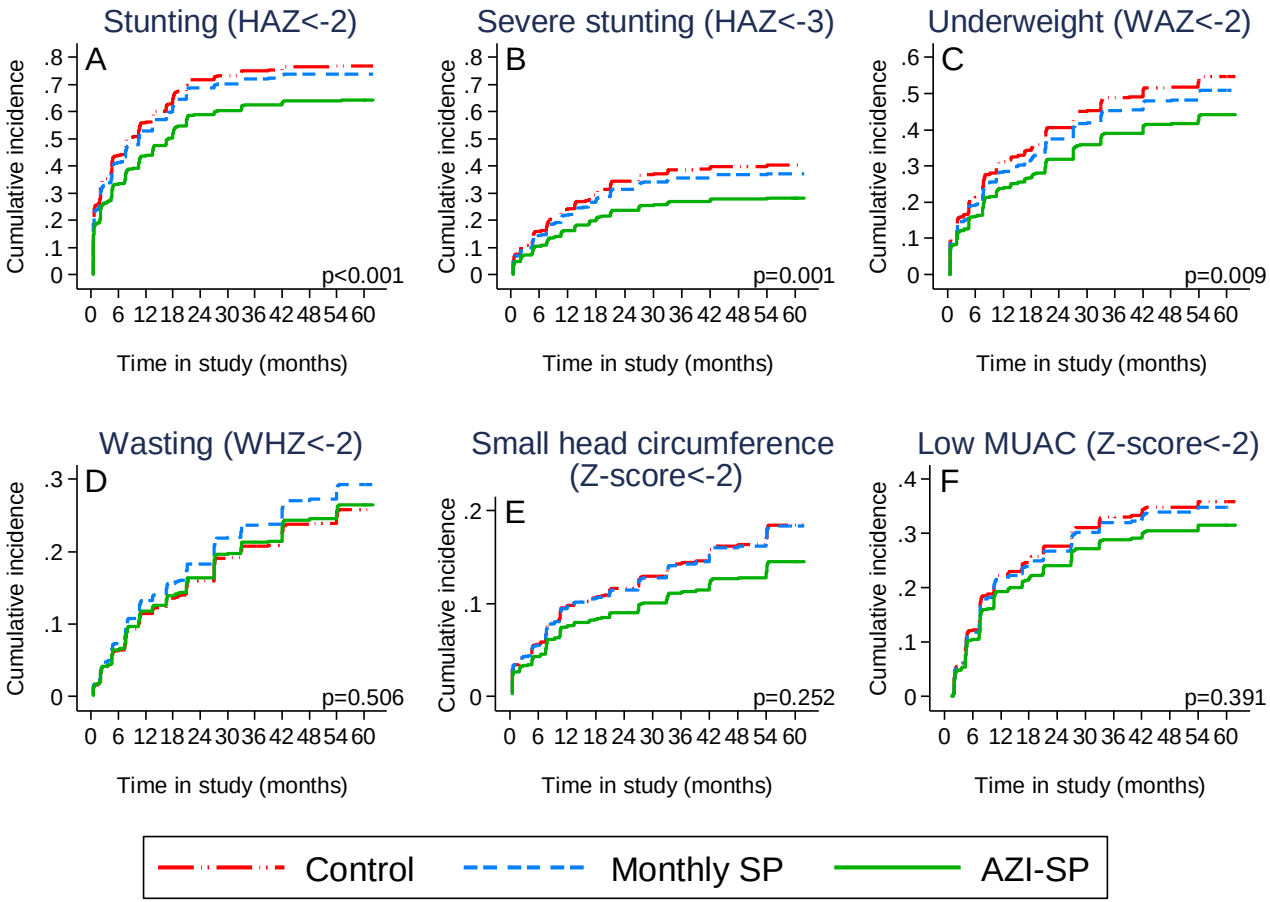
Table 6. Prevalence of Various Forms of Undernutrition by Intervention Group at 6, 12, 24, 36, 48, and 60 Months of Age

Outcome	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
		Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Prevalence of moderate to severe stunting (HAZ < -2)	6 mo	31.8% (114/359)	26.2% (95/362)	24.2% (90/372)	0.061	0.76 (0.60 to 0.97)	0.024	0.92 (0.72 to 1.18)	0.524	0.83 (0.66 to 1.04)	0.107
	12 mo	43.3% (148/342)	36.1% (126/349)	32.6% (118/362)	0.011	0.75 (0.62 to 0.91)	0.004	0.90 (0.74 to 1.11)	0.326	0.83 (0.69 to 1.00)	0.056
	24 mo	61.0% (206/338)	54.2% (189/349)	51.1% (180/352)	0.027	0.84 (0.73 to 0.96)	0.010	0.94 (0.82 to 1.09)	0.425	0.89 (0.78 to 1.01)	0.074
	36 mo	54.1% (178/329)	49.3% (165/335)	43.2% (153/354)	0.019	0.80 (0.68 to 0.93)	0.005	0.88 (0.75 to 1.03)	0.114	0.91 (0.78 to 1.06)	0.215
	48 mo	43.5% (144/331)	42.4% (140/330)	38.0% (127/334)	0.326	0.87 (0.73 to 1.05)	0.153	0.90 (0.74 to 1.08)	0.250	0.98 (0.82 to 1.16)	0.781
	60 mo	36.8% (116/315)	35.9% (112/312)	31.1% (101/325)	0.270	0.84 (0.68 to 1.05)	0.127	0.87 (0.69 to 1.08)	0.200	0.97 (0.79 to 1.20)	0.811
Prevalence of severe stunting (HAZ < -3)	6 mo	9.8% (35/359)	9.7% (35/362)	7.8% (29/372)	0.583	0.80 (0.50 to 1.28)	0.351	0.81 (0.50 to 1.29)	0.369	0.99 (0.64 to 1.55)	0.971
	12 mo	11.4% (39/342)	13.5% (47/349)	9.9% (36/362)	0.339	0.87 (0.57 to 1.34)	0.531	0.74 (0.49 to 1.11)	0.145	1.18 (0.79 to 1.76)	0.412
	24 mo	18.1% (61/338)	23.2% (81/349)	13.6% (48/352)	0.005	0.76 (0.53 to 1.07)	0.114	0.59 (0.42 to 0.81)	0.001	1.29 (0.95 to 1.73)	0.098
	36 mo	15.8% (52/329)	17.9% (60/335)	11.6% (41/354)	0.065	0.73 (0.50 to 1.08)	0.112	0.65 (0.45 to 0.93)	0.020	1.13 (0.81 to 1.59)	0.473
	48 mo	11.8% (39/331)	10.3% (34/330)	8.7% (29/334)	0.430	0.74 (0.46 to 1.17)	0.194	0.84 (0.53 to 1.35)	0.477	0.87 (0.56 to 1.36)	0.548
	60 mo	7.6% (24/315)	7.7% (24/312)	7.1% (23/325)	0.949	0.93 (0.53 to 1.63)	0.797	0.92 (0.53 to 1.59)	0.766	1.01 (0.58 to 1.76)	0.973
Prevalence of moderate to severe underweight (WAZ < -2)	6 mo	13.8% (50/363)	14.0% (51/364)	9.1% (34/374)	0.078	0.66 (0.44 to 1.00)	0.048	0.65 (0.43 to 0.98)	0.038	1.02 (0.71 to 1.46)	0.926
	12 mo	16.6% (57/343)	15.9% (55/347)	16.3% (59/362)	0.964	0.98 (0.70 to 1.37)	0.909	1.03 (0.73 to 1.44)	0.872	0.95 (0.68 to 1.34)	0.786
	24 mo	24.2% (81/335)	24.7% (85/344)	21.1% (73/346)	0.489	0.87 (0.66 to 1.16)	0.342	0.85 (0.65 to 1.12)	0.261	1.02 (0.78 to 1.34)	0.874
	36 mo	23.9% (78/326)	23.6% (78/331)	21.1% (74/351)	0.634	0.88 (0.66 to 1.17)	0.381	0.89 (0.68 to 1.18)	0.436	0.98 (0.75 to 1.30)	0.914
	48 mo	22.2% (73/329)	23.4% (76/325)	22.4% (74/331)	0.925	1.01 (0.76 to 1.34)	0.959	0.96 (0.72 to 1.27)	0.754	1.05 (0.79 to 1.40)	0.718
	60 mo	20.1% (63/314)	19.4% (60/309)	16.5% (53/321)	0.479	0.82 (0.59 to 1.15)	0.250	0.85 (0.61 to 1.19)	0.342	0.97 (0.70 to 1.33)	0.840
Prevalence of severe underweight (WAZ < -3)	6 mo	3.9% (14/363)	5.0% (18/364)	2.1% (8/374)	0.134	0.55 (0.24 to 1.31)	0.178	0.43 (0.19 to 0.98)	0.045	1.28 (0.65 to 2.54)	0.475
	12 mo	5.0% (17/343)	5.2% (18/347)	3.6% (13/362)	0.550	0.72 (0.36 to 1.47)	0.372	0.69 (0.34 to 1.39)	0.302	1.05 (0.55 to 2.00)	0.890
	24 mo	4.8% (16/335)	6.4% (22/344)	4.9% (17/346)	0.581	1.03 (0.53 to 2.00)	0.934	0.77 (0.42 to 1.42)	0.401	1.34 (0.72 to 2.50)	0.361
	36 mo	4.0% (13/326)	4.8% (16/331)	4.6% (16/351)	0.878	1.14 (0.54 to 2.41)	0.725	0.94 (0.48 to 1.86)	0.865	1.21 (0.58 to 2.55)	0.613
	48 mo	4.0% (13/329)	3.7% (12/325)	5.4% (18/331)	0.505	1.38 (0.67 to 2.84)	0.388	1.47 (0.72 to 3.01)	0.288	0.93 (0.42 to 2.07)	0.867
	60 mo	2.9% (9/314)	4.9% (15/309)	5.6% (18/321)	0.237	1.96 (0.89 to 4.28)	0.093	1.16 (0.59 to 2.25)	0.672	1.69 (0.75 to 3.81)	0.203

Outcome	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
		Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Prevalence of moderate to severe wasting (WHZ < -2)	6 mo	2.2% (8/358)	3.6% (13/360)	2.7% (10/371)	0.533	1.21 (0.48 to 3.02)	0.689	0.75 (0.33 to 1.68)	0.480	1.62 (0.68 to 3.85)	0.279
	12 mo	4.7% (16/341)	5.2% (18/347)	4.4% (16/362)	0.889	0.94 (0.48 to 1.85)	0.863	0.85 (0.44 to 1.64)	0.633	1.11 (0.57 to 2.13)	0.765
	24 mo	5.4% (18/335)	5.3% (18/343)	4.9% (17/346)	0.962	0.91 (0.48 to 1.74)	0.786	0.94 (0.49 to 1.78)	0.841	0.98 (0.52 to 1.84)	0.942
	36 mo	7.1% (23/325)	7% (23/331)	5.1% (18/351)	0.515	0.72 (0.39 to 1.33)	0.300	0.74 (0.41 to 1.34)	0.320	0.98 (0.56 to 1.73)	0.950
	48 mo	5.2% (17/329)	7.7% (25/325)	6.7% (22/331)	0.450	1.29 (0.68 to 2.42)	0.436	0.86 (0.50 to 1.50)	0.604	1.49 (0.80 to 2.76)	0.206
	60 mo	6.8% (21/307)	6.2% (19/305)	6.3% (20/318)	0.944	0.92 (0.51 to 1.66)	0.781	1.01 (0.55 to 1.86)	0.975	0.91 (0.50 to 1.66)	0.760
Prevalence of severe wasting (WHZ < -3)	6 mo	0.0% (0/358)	0.6% (2/360)	0.0% (0/371)	NA	NA	NA	NA	NA	NA	NA
	12 mo	0.3% (1/341)	0.9% (3/347)	0.6% (2/362)	0.631	1.88 (0.17 to 20.71)	0.605	0.64 (0.11 to 3.8)	0.623	2.95 (0.31 to 28.23)	0.348
	24 mo	1.5% (5/335)	1.8% (6/343)	0.9% (3/346)	0.602	0.58 (0.14 to 2.41)	0.455	0.50 (0.12 to 1.97)	0.318	1.17 (0.36 to 3.81)	0.792
	36 mo	0.9% (3/325)	0.3% (1/331)	0.3% (1/351)	0.452	0.31 (0.03 to 2.95)	0.307	0.94 (0.06 to 15.04)	0.967	0.33 (0.03 to 3.13)	0.332
	48 mo	1.5% (5/329)	0.9% (3/325)	0.9% (3/331)	0.701	0.60 (0.14 to 2.48)	0.477	0.98 (0.20 to 4.83)	0.982	0.61 (0.15 to 2.52)	0.493
	60 mo	0.7% (2/307)	1.6% (5/305)	1.9% (6/318)	0.415	2.90 (0.59 to 14.25)	0.191	1.15 (0.35 to 3.73)	0.815	2.52 (0.49 to 12.88)	0.268
Prevalence of small head circumference (head circumference-for-age z-score < -2)	6 mo	2.2% (8/363)	2.5% (9/362)	1.6% (6/372)	0.704	0.73 (0.26 to 2.09)	0.560	0.65 (0.23 to 1.81)	0.407	1.13 (0.44 to 2.89)	0.802
	12 mo	3.5% (12/340)	5.2% (18/349)	3.6% (13/359)	0.480	1.03 (0.47 to 2.22)	0.948	0.70 (0.35 to 1.41)	0.321	1.46 (0.71 to 2.99)	0.299
	24 mo	2.4% (8/338)	5.2% (18/349)	4% (14/351)	0.176	1.69 (0.72 to 3.97)	0.232	0.77 (0.39 to 1.53)	0.461	2.18 (0.96 to 4.95)	0.063
	36 mo	4.9% (16/328)	5.4% (18/335)	5.4% (19/353)	0.946	1.10 (0.58 to 2.11)	0.766	1.00 (0.53 to 1.88)	0.996	1.10 (0.57 to 2.12)	0.773
	48 mo	7.0% (23/331)	8.5% (28/330)	3.9% (13/333)	0.059	0.56 (0.29 to 1.09)	0.088	0.46 (0.24 to 0.87)	0.018	1.22 (0.72 to 2.08)	0.461
	60 mo	9.1% (28/307)	8.8% (27/308)	5.9% (19/320)	0.278	0.65 (0.37 to 1.14)	0.134	0.68 (0.38 to 1.19)	0.177	0.96 (0.58 to 1.59)	0.878
Prevalence of very small head circumference (head circumference-for-age z-score < -3)	6 mo	0.8% (3/363)	0.3% (1/362)	0.3% (1/372)	0.476	0.33 (0.03 to 3.12)	0.330	0.97 (0.06 to 15.52)	0.985	0.33 (0.03 to 3.20)	0.342
	12 mo	1.5% (5/340)	0.6% (2/349)	1.1% (4/359)	0.528	0.76 (0.21 to 2.80)	0.677	1.94 (0.36 to 10.56)	0.441	0.39 (0.08 to 2.00)	0.258
	24 mo	0.3% (1/338)	0.3% (1/349)	0.6% (2/351)	0.797	1.93 (0.18 to 21.17)	0.592	1.99 (0.18 to 21.86)	0.574	0.97 (0.06 to 15.44)	0.982
	36 mo	0.3% (1/328)	0.0% (0/335)	0.6% (2/353)	0.612	1.86 (0.17 to 20.43)	0.612	NA	NA	NA	NA
	48 mo	0.3% (1/331)	0.9% (3/330)	0.6% (2/333)	0.625	1.99 (0.18 to 21.85)	0.574	0.66 (0.11 to 3.93)	0.649	3.01 (0.31 to 28.81)	0.339
	60 mo	1.0% (3/307)	0.3% (1/308)	0.6% (2/320)	0.621	0.64 (0.11 to 3.81)	0.623	1.93 (0.18 to 21.15)	0.592	0.33 (0.03 to 3.18)	0.339

Outcome	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
		Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Prevalence of low MUAC (MUAC-for-age z-score < -2)	6 mo	11.1% (40/362)	10.2% (37/364)	8.0% (30/375)	0.360	0.72 (0.46 to 1.14)	0.161	0.79 (0.50 to 1.25)	0.307	0.92 (0.60 to 1.40)	0.699
	12 mo	11.6% (40/344)	13.8% (48/349)	12.4% (45/362)	0.700	1.07 (0.72 to 1.59)	0.743	0.90 (0.62 to 1.33)	0.605	1.18 (0.80 to 1.76)	0.405
	24 mo	11.0% (37/337)	11.4% (40/350)	8.8% (31/352)	0.484	0.80 (0.51 to 1.27)	0.346	0.77 (0.49 to 1.20)	0.251	1.04 (0.68 to 1.59)	0.854
	36 mo	10.3% (34/330)	9.0% (30/335)	9.0% (32/354)	0.806	0.88 (0.55 to 1.40)	0.581	1.01 (0.63 to 1.62)	0.969	0.87 (0.54 to 1.39)	0.561
	48 mo	10.3% (34/331)	10.0% (33/330)	10.8% (36/334)	0.946	1.05 (0.67 to 1.65)	0.834	1.08 (0.69 to 1.69)	0.743	0.97 (0.61 to 1.54)	0.909
	60 mo	9.4% (29/308)	9.4% (29/310)	11.2% (36/322)	0.687	1.19 (0.74 to 1.90)	0.475	1.20 (0.75 to 1.90)	0.451	0.99 (0.60 to 1.63)	0.980
Prevalence of very low MUAC (MUAC-for-age z-score < -3)	6 mo	2.2% (8/362)	3.9% (14/364)	1.3% (5/375)	0.097	0.60 (0.20 to 1.83)	0.372	0.35 (0.13 to 0.95)	0.040	1.74 (0.74 to 4.10)	0.205
	12 mo	3.2% (11/344)	2.6% (9/349)	3% (11/362)	0.882	0.95 (0.42 to 2.16)	0.903	1.18 (0.49 to 2.81)	0.711	0.81 (0.34 to 1.92)	0.628
	24 mo	0.9% (3/337)	2.0% (7/350)	1.4% (5/352)	0.489	1.60 (0.38 to 6.63)	0.520	0.71 (0.23 to 2.21)	0.555	2.25 (0.59 to 8.61)	0.238
	36 mo	2.7% (9/330)	0.6% (2/335)	1.4% (5/354)	0.132	0.52 (0.17 to 1.59)	0.251	2.37 (0.46 to 12.12)	0.302	0.22 (0.05 to 1.04)	0.055
	48 mo	0.9% (3/331)	0.9% (3/330)	1.2% (4/334)	0.911	1.32 (0.30 to 5.85)	0.713	1.32 (0.30 to 5.85)	0.717	1.00 (0.20 to 4.93)	0.997
	60 mo	0.7% (2/308)	0.7% (2/310)	0.6% (2/322)	0.999	0.96 (0.14 to 6.76)	0.964	0.96 (0.14 to 6.80)	0.970	0.99 (0.14 to 7.02)	0.995

Figure 7. Cumulative Incidence of Stunting, Severe Stunting, Underweight, Wasting, Small Head Circumference, and MUAC



Cumulative incidence of stunting (HAZ < -2) (panel A), severe stunting (HAZ < -3) (panel B), underweight (WAZ < -2) (panel C), wasting (WHZ < -2) (panel D), small head circumference (head circumference-for-age z-score < -2) (panel E), and low MUAC (MUAC-for-age z-score < -2) (panel F) by 60 months of age by intervention group.

3.4.3 Covariate Adjustment, Interaction Tests, and Sensitivity Analyses

Adjustment for maternal malaria at enrollment, HIV status, height, BMI, number of previous pregnancies, number of school years, and child sex did not markedly change the mean difference in z-scores between groups or the prevalence of the different types of malnutrition (details not shown). Out of 118 tests for interaction carried out with growth outcomes, without including covariates in the models, 18 (15.3%) were statistically significant ($p < 0.1$) (Appendix 2, Supplementary Table 4). The results did not show a clear pattern as to how the effect of the intervention was modified by other variables (Appendix 2, Supplementary Tables 5 and 6). Because of the small number of children with severe wasting (n = 14), very small head circumference (n = 4), and very low MUAC (n = 15) at 24 months, these outcomes were omitted from the interaction testing.

Sensitivity analyses with multiple imputed data to replace weight measurements rounded to the full kilogram and to control for missing anthropometric data gave similar results compared to those with unimputed data (results not shown). Descriptive statistics of imputed data by child sex were compared to the original data without imputations, and all three datasets were comparable (Appendix 3, Supplementary Table 8).

3.5 Development

The mean (SD) total developmental score of children in the study cohort was 110.6 (17.3) points; mean (SD) for locomotor subscale was 24.8 (3.8), personal-social subscale was 27.2 (3.9), language subscale was 15.1 (5.0), eye and hand coordination subscale was 8.7 (3.2), performance subscale was 15.8 (6.1), and practical reasoning subscale was 18.9 (3.7) points. Group-wise, the mean (SD) total developmental score was 108.8 (17.1) in the control group, 110.3 (17.0) in the monthly SP group, and 112.5 (17.6) in the AZI-SP group ($p = 0.029$). Compared to the control group, the AZI-SP group had a 3.7 (95% CI 1.0 to 6.4) point higher mean total developmental score than the control group ($p = 0.008$) (Table 7a). For the performance subscale, the difference in means between the AZI-SP group and the control group was 1.7 (95% CI 0.7 to 2.7) points ($p = 0.001$, Holm's adjusted $p = 0.006$) (Table 7f). For the other developmental subscales, children in the AZI-SP group had a 0.1–0.8 point higher mean scores than children in the control group, but these differences were not statistically significant ($p > 0.05$, Tables 7b-g).

Adjustment of the models for maternal education and a household assets index did not markedly change the associations between the intervention group and the developmental scores (details not shown). The other variables that were considered possible confounders (see methods section 2.6.2.1) were not associated with the total developmental score and therefore were not included in the models.

Adjustment of the models for potential intermediary outcomes (an attenuation analysis) decreased but did not eliminate the association between the intervention and the total developmental score (Table 7a). Adjustment to the subscale scores for the same potential intermediary outcomes either did not reduce or reduced slightly the strength of the association between the intervention and the subscale score, but for these analyses, the differences between intervention groups were mostly not statistically significant either before or after the adjustment for potential intermediary outcomes (Tables 7b-g).

Out of a total of 10 tests for interaction, two (20%) gave statistically significant results ($p < 0.1$) (Appendix 2, Supplementary Table 7). Tests for interactions indicated that the number of previous pregnancies, maternal malaria at enrollment, maternal HIV status, maternal BMI, maternal age, years of education, Hb at enrollment, and child sex did not modify the association between the intervention and total developmental score.

The association between the intervention and total developmental score was modified by the duration of pregnancy at enrollment ($p = 0.028$) (Table 8). Among children who were born to mothers who had a duration of pregnancy above the median at enrollment, the mean (SD) total developmental score was 106.9 (18.5) in the control group, 110.1 (16.8) in the monthly SP group, and 113.5 (18.5) in the AZI-SP group ($p = 0.005$). The difference in mean developmental score was 6.7 (95% CI 2.6 to 10.7) points higher in the AZI-SP group compared to the control group ($p = 0.001$). Among children born to mothers who had a duration of pregnancy at or below the median at enrollment, the mean (SD) total developmental score was almost the same in all groups: 110.9 (15.1) in the control group, 110.5 (17.1) in the monthly SP group, and 111.6 (16.6) in the AZI-SP group ($p = 0.841$).

The association between the intervention and total developmental score was modified by maternal height at enrollment ($p = 0.089$) (Table 8). Among children who were born to mothers who had height above the median, mean (SD) total developmental score was 107.0 (17.4) in the control group, 110.1 (16.2) in the monthly SP group, and 114.2 (17.1) in the AZI-SP group ($p = 0.001$). The difference in mean total developmental score was 7.1 (95% CI 3.4 to 10.9) points higher in the AZI-SP group compared to the control group ($p < 0.001$). Among children born to mothers who had height at or below the median, the mean (SD) total developmental score was almost the same in all groups: 110.6 (17.7) in the control group, 110.5 (17.7) in the monthly SP group, and 110.6 (18.1) in the AZI-SP group ($p = 0.998$).

Sensitivity analysis with unimputed data gave similar results compared to those with imputed data. The differences between intervention groups were approximately the same size for total developmental score and all the subscales (results not shown). Descriptive statistics of imputed data by child sex were compared to the original data without imputations, and both datasets were comparable (Appendix 3, Supplementary Table 9).

The validation analysis showed that maternal education, household asset index, HAZ at 1 month of age and at 5 years of age, and head circumference-for-age z-score at 1 month of age and at 5 years of age—but not household size or duration of pregnancy—were associated with total developmental score at 5 years of age (Table 9). After fitting a multiple variable regression model with all explanatory characteristics in the same model, the results remained the same except that HAZ and head circumference-for-age z-score at 1 month of age were no longer statistically significant ($p \geq 0.05$) (Table 9).

Table 7a. Total Developmental Score, Mean (SD), by Intervention Group at 60 Months of Age

(All models adjusted for child sex and age at the time of developmental assessment)

Outcome	Mean (SD[1])				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
	Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value
Total score	108.8 (17.1)	110.3 (17.0)	112.5 (17.6)	0.029	3.7 (1.0 to 6.4)	0.008	2.2 (-0.6 to 4.9)	0.123	1.6 (-1.2 to 4.3)	0.260
Total score, adjusted for duration of pregnancy	108.8 (17.1)	110.4 (17.0)	112.2 (17.6)	0.042	3.6 (0.8 to 6.3)	0.011	2.1 (-0.6 to 4.8)	0.135	1.5 (-1.2 to 4.2)	0.278
Total score, adjusted for birth weight	109.0 (17.1)	110.4 (16.9)	112.2 (17.4)	0.080	3.2 (0.4 to 6.0)	0.025	1.9 (-0.8 to 4.6)	0.176	1.3 (-1.4 to 4.0)	0.349
Total score, adjusted for HAZ at 1 month	109.0 (17.1)	110.4 (16.8)	112.3 (17.5)	0.068	3.3 (0.5 to 6.0)	0.021	1.9 (-0.8 to 4.6)	0.166	1.3 (-1.4 to 4.1)	0.332
Total score, adjusted for head circumference-for-age z-score at 1 month	109.0 (17.0)	110.5 (16.8)	112.1 (17.5)	0.089	3.1 (0.3 to 5.9)	0.027	1.6 (-1.1 to 4.3)	0.255	1.5 (-1.2 to 4.2)	0.269
Total score, adjusted for length-for-gestational age	109.0 (17.1)	110.5 (16.6)	112.4 (17.5)	0.051	3.4 (0.7 to 6.2)	0.014	1.9 (-0.8 to 4.6)	0.178	1.6 (-1.1 to 4.3)	0.258
Total score, adjusted for weight-for-gestational age	109.0 (17.1)	110.5 (16.7)	112.4 (17.4)	0.062	3.3 (0.6 to 6.1)	0.018	1.8 (-0.9 to 4.5)	0.190	1.5 (-1.2 to 4.2)	0.276
Total score, adjusted for head circumference-for-gestational age	109.1 (17.1)	110.6 (16.7)	112.2 (17.4)	0.089	3.1 (0.4 to 5.9)	0.026	1.6 (-1.1 to 4.4)	0.238	1.5 (-1.2 to 4.2)	0.286

[1] SD for multiple imputed data calculated as an average SD from 50 imputations.

Table 7b. Locomotor Score, Mean (SD), by Intervention Group at 60 Months of Age

(All models adjusted for child sex and age at the time of developmental assessment)

Outcome	Mean (SD[1])				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
	Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	p-value	Diff. in means (95% CI)	p-value	Diff. in means (95% CI)	p-value
Locomotor score	24.7 (3.8)	24.9 (3.6)	24.9 (3.9)	0.862	0.1 (-0.5 to 0.7)	0.667	0.0 (-0.6 to 0.6)	0.945	0.2 (-0.4 to 0.7)	0.610
Locomotor score, adjusted for duration of pregnancy	24.8 (3.8)	24.9 (3.6)	24.8 (3.9)	0.914	0.1 (-0.5 to 0.7)	0.828	-0.1 (-0.6 to 0.5)	0.844	0.1 (-0.5 to 0.7)	0.672
Locomotor score, adjusted for birth weight	24.8 (3.9)	24.9 (3.5)	24.8 (3.9)	0.941	0.0 (-0.6 to 0.6)	0.986	-0.1 (-0.6 to 0.5)	0.776	0.1 (-0.5 to 0.7)	0.763
Locomotor score, adjusted for HAZ at 1 month	24.8 (3.8)	24.9 (3.5)	24.8 (3.9)	0.934	0.0 (-0.6 to 0.6)	0.948	-0.1 (-0.7 to 0.5)	0.790	0.1 (-0.5 to 0.7)	0.740
Locomotor score, adjusted for head circumference-for-age z-score at 1 month	24.8 (3.8)	24.9 (3.5)	24.8 (3.9)	0.853	0.0 (-0.6 to 0.6)	0.991	-0.1 (-0.7 to 0.4)	0.636	0.1 (-0.4 to 0.7)	0.627
Locomotor score, adjusted for length-for-gestational age	24.8 (3.9)	24.9 (3.6)	24.8 (3.9)	0.879	0.1 (-0.5 to 0.7)	0.817	-0.1 (-0.7 to 0.5)	0.787	0.2 (-0.4 to 0.7)	0.614
Locomotor score, adjusted for weight-for-gestational age	24.8 (3.9)	24.9 (3.6)	24.8 (3.9)	0.886	0.1 (-0.5 to 0.7)	0.844	-0.1 (-0.7 to 0.5)	0.776	0.1 (-0.4 to 0.7)	0.628
Locomotor score, adjusted for head circumference-for-gestational age	24.8 (3.9)	24.9 (3.6)	24.8 (3.9)	0.877	0.0 (-0.7 to 0.6)	0.905	-0.1 (-0.7 to 0.5)	0.717	0.1 (-0.4 to 0.7)	0.627

[1] SD for multiple imputed data calculated as an average SD from 50 imputations.

Table 7c. Personal-Social Score, Mean (SD), by Intervention Group at 60 Months of Age

(All models adjusted for child sex and age at the time of developmental assessment)

Outcome	Mean (SD[1])				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
	Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	p-value	Diff. in means (95% CI)	p-value	Diff. in means (95% CI)	p-value
Personal-social score	27.0 (4.0)	27.3 (4.0)	27.4 (3.9)	0.346	0.4 (-0.2 to 1.0)	0.189	0.0 (-0.6 to 0.7)	0.922	0.4 (-0.2 to 1.0)	0.228
Personal-social score, adjusted for duration of pregnancy	27.0 (4.0)	27.3 (4.0)	27.4 (3.9)	0.367	0.4 (-0.2 to 1.0)	0.203	0.0 (-0.6 to 0.6)	0.933	0.4 (-0.3 to 1.0)	0.235
Personal-social score, adjusted for birth weight	27.0 (4.0)	27.3 (4.0)	27.3 (3.8)	0.455	0.4 (-0.3 to 1.1)	0.196	0.0 (-0.6 to 0.6)	0.935	0.4 (-0.3 to 1.0)	0.223
Personal-social score, adjusted for HAZ at 1 month	27.0 (4.0)	27.3 (4.0)	27.4 (3.9)	0.416	0.4 (-0.3 to 1.0)	0.240	0.0 (-0.6 to 0.6)	0.971	0.4 (-0.3 to 1.0)	0.255
Personal-social score, adjusted for head circumference-for-age z-score at 1 month	27.0 (4.0)	27.4 (4.0)	27.3 (3.9)	0.418	0.4 (-0.3 to 1.0)	0.268	0.0 (-0.6 to 0.6)	0.936	0.4 (-0.2 to 1.0)	0.233
Personal-social score, adjusted for length-for-gestational age	27.0 (4.0)	27.4 (3.9)	27.4 (3.9)	0.351	0.4 (-0.2 to 1.0)	0.217	0.0 (-0.6 to 0.6)	0.961	0.4 (-0.2 to 1.0)	0.199
Personal-social score, adjusted for weight-for-gestational age	27.0 (4.0)	27.4 (3.9)	27.4 (3.8)	0.389	0.4 (-0.3 to 1.0)	0.249	0.0 (-0.6 to 0.6)	0.936	0.4 (-0.2 to 1.0)	0.216
Personal-social score, adjusted for head circumference-for-gestational age	27.0 (4.0)	27.4 (3.9)	27.4 (3.9)	0.368	0.4 (-0.3 to 1.0)	0.238	0.0 (-0.7 to 0.6)	0.933	0.4 (-0.2 to 1.0)	0.204

[1] SD for multiple imputed data calculated as an average SD from 50 imputations.

Table 7d. Language Score, Mean (SD), by Intervention Group at 60 Months of Age

(All models adjusted for child sex and age at the time of developmental assessment)

Outcome	Mean (SD[1])				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
	Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	p-value	Diff. in means (95% CI)	p-value	Diff. in means (95% CI)	p-value
Language score	14.6 (5.0)	15.0 (5.1)	15.5 (4.8)	0.102	0.8 (0.1 to 1.6)	0.033	0.5 (-0.3 to 1.3)	0.235	0.4 (-0.4 to 1.1)	0.369
Language score, adjusted for duration of pregnancy	14.5 (5.0)	15.0 (5.1)	15.5 (4.8)	0.090	0.9 (0.1 to 1.7)	0.029	0.5 (-0.3 to 1.3)	0.220	0.4 (-0.4 to 1.2)	0.356
Language score, adjusted for birth weight	14.7 (5.0)	15.0 (5.1)	15.5 (4.8)	0.134	0.8 (-0.0 to 1.6)	0.045	0.5 (-0.3 to 1.3)	0.260	0.3 (-0.5 to 1.1)	0.402
Language score, adjusted for HAZ at 1 month	14.7 (5.0)	15.0 (5.1)	15.5 (4.8)	0.125	0.8 (0.0 to 1.6)	0.042	0.5 (-0.3 to 1.3)	0.252	0.3 (-0.4 to 1.1)	0.392
Language score, adjusted for head circumference-for-age z-score at 1 month	14.7 (5.0)	15.0 (5.1)	15.5 (4.8)	0.145	0.8 (0.0 to 1.6)	0.050	0.4 (-0.4 to 1.2)	0.292	0.4 (-0.4 to 1.1)	0.374
Language score, adjusted for length-for-gestational age	14.7 (5.0)	15.0 (5.0)	15.5 (4.8)	0.155	0.8 (-0.0 to 1.5)	0.054	0.4 (-0.4 to 1.2)	0.284	0.3 (-0.5 to 1.1)	0.415
Language score, adjusted for weight-for-gestational age	14.7 (5.0)	15.0 (5.0)	15.4 (4.8)	0.174	0.7 (-0.0 to 1.5)	0.062	0.4 (-0.4 to 1.2)	0.295	0.3 (-0.5 to 1.1)	0.437
Language score, adjusted for head circumference-for-gestational age	14.7 (5.0)	15.0 (5.0)	15.5 (4.8)	0.164	0.8 (-0.0 to 1.6)	0.057	0.4 (-0.4 to 1.2)	0.292	0.3 (-0.5 to 1.1)	0.412

[1] SD for multiple imputed data calculated as an average SD from 50 imputations.

Table 7e. Eye and Hand Coordination Score, Mean (SD), by Intervention Group at 60 Months of Age

(All models adjusted for child sex and age at the time of developmental assessment)

Outcome	Mean (SD[1])				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
	Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	p-value	Diff. in means (95% CI)	p-value	Diff. in means (95% CI)	p-value
Eye and hand coordination score	8.5 (3.2)	9.0 (3.3)	8.7 (3.0)	0.134	0.2 (-0.3 to 0.7)	0.352	-0.3 (-0.8 to 0.2)	0.258	0.5 (0.0 to 1.0)	0.042
Eye and hand coordination score, adjusted for duration of pregnancy	8.5 (3.2)	9.0 (332)	8.7 (3.0)	0.147	0.2 (-0.3 to 0.7)	0.467	-0.3 (-0.8 to 0.2)	0.214	0.5 (0.0 to 1.0)	0.050
Eye and hand coordination score, adjusted for birth weight	8.5 (3.2)	9.0 (3.3)	8.7 (3.0)	0.163	0.2 (-0.3 to 0.6)	0.534	-0.3 (-0.8 to 0.2)	0.200	0.5 (-0.0 to 1.0)	0.059
Eye and hand coordination score, adjusted for HAZ at 1 month	8.5 (3.2)	9.0 (3.2)	8.7 (3.0)	0.163	0.1 (-0.4 to 0.6)	0.590	-0.3 (-0.8 to 0.2)	0.182	0.5 (-0.0 to 1.0)	0.061
Eye and hand coordination score, adjusted for head circumference-for-age z-score at 1 month	8.5 (3.2)	9.0 (3.3)	8.6 (3.0)	0.116	0.1 (-0.4 to 0.6)	0.602	-0.4 (-0.9 to 0.1)	0.136	0.5 (0.0 to 1.0)	0.043
Eye and hand coordination score, adjusted for length-for-gestational age	8.5 (3.2)	9.0 (3.3)	8.7 (3.0)	0.177	0.2 (-0.3 to 0.7)	0.487	-0.3 (-0.8 to 0.2)	0.233	0.5 (-0.0 to 0.9)	0.062
Eye and hand coordination score, adjusted for weight-for-gestational age	8.5 (3.2)	9.0 (3.3)	8.7 (3.0)	0.172	0.2 (-0.3 to 0.7)	0.453	-0.3 (0.2 to 0.8)	0.243	0.5 (-0.0 to 1.0)	0.059
Eye and hand coordination score, adjusted for head circumference-for-gestational age	8.5 (3.2)	9.0 (3.3)	8.7 (3.0)	0.185	0.1 (-0.4 to 0.6)	0.657	-0.3 (-0.8 to 0.2)	0.175	0.5 (-0.0 to 0.9)	0.075

[1] SD for multiple imputed data calculated as an average SD from 50 imputations.

Table 7f. Performance Score, Mean (SD), by Intervention Group at 60 Months of Age

(All models adjusted for child sex and age at the time of developmental assessment)

Outcome	Mean (SD[1])				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
	Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	p-value	Diff. in means (95% CI)	p-value	Diff. in means (95% CI)	p-value
Performance score	15.1 (6.2)	15.4 (5.9)	16.9 (6.1)	0.001	1.7 (0.7 to 2.7)	0.001	1.5 (0.5 to 2.4)	0.003	0.3 (-0.7 to 1.3)	0.580
Performance score, adjusted for duration of pregnancy	15.1 (6.2)	15.4 (5.9)	16.8 (6.1)	0.001	1.7 (0.7 to 2.7)	0.001	1.4 (0.5 to 2.4)	0.003	0.3 (-0.7 to 1.2)	0.609
Performance score, adjusted for birth weight	15.2 (6.2)	15.4 (5.9)	16.8 (6.1)	0.003	1.6 (0.6 to 2.6)	0.002	1.4 (0.4 to 2.3)	0.004	0.2 (-0.8 to 1.2)	0.664
Performance score, adjusted for HAZ at 1 month	15.2 (6.2)	15.4 (5.8)	16.8 (6.1)	0.002	1.6 (0.6 to 2.6)	0.001	1.4 (0.4 to 2.3)	0.004	0.2 (-0.8 to 1.2)	0.659
Performance score, adjusted for head circumference-for-age z-score at 1 month	15.2 (6.2)	15.5 (5.9)	16.7 (6.1)	0.004	1.6 (0.6 to 2.5)	0.002	1.3 (0.3 to 2.2)	0.008	0.3 (-0.7 to 1.2)	0.593
Performance score, adjusted for length-for-gestational age	15.2 (6.2)	15.5 (5.8)	16.9 (6.1)	0.001	1.7 (0.7 to 2.7)	0.002	1.4 (0.4 to 2.3)	0.011	0.3 (-0.6 to 1.3)	0.458
Performance score, adjusted for weight-for-gestational age	15.2 (6.2)	15.5 (5.8)	16.9 (6.1)	0.002	1.7 (0.7 to 2.7)	0.001	1.4 (0.4 to 2.3)	0.005	0.3 (-0.7 to 1.3)	0.512
Performance score, adjusted for head circumference-for-gestational age	15.2 (6.2)	15.5 (5.8)	16.8 (6.1)	0.004	1.6 (0.6 to 2.6)	0.002	1.3 (0.3 to 2.2)	0.008	0.3 (-0.7 to 1.3)	0.560

[1] SD for multiple imputed data calculated as an average SD from 50 imputations.

Table 7g. Practical Reasoning Score, Mean (SD), by Intervention Group at 60 Months of Age

(All models adjusted for child sex and age at the time of developmental assessment)

	Mean (SD[1])				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
Outcome	**Control**	**Monthly SP**	**AZI-SP**	**Overall p-value**	**Diff. in means (95% CI)**	**p-value**	**Diff. in means (95% CI)**	**p-value**	**Diff. in means (95% CI)**	**p-value**
Practical reasoning score	18.9 (3.7)	18.7 (3.7)	19.2 (3.7)	0.245	0.4 (-0.2 to 0.9)	0.226	0.5 (-0.1 to 1.1)	0.106	-0.1 (-0.7 to 0.5)	0.682
Practical reasoning score, adjusted for duration of pregnancy	18.8 (3.7)	18.7 (3.7)	19.2 (3.7)	0.229	0.4 (-0.2 to 1.0)	0.211	0.5 (-0.1 to 1.1)	0.099	-0.1 (-0.7 to 0.5)	0.699
Practical reasoning score, adjusted for birth weight	18.9 (3.7)	18.7 (3.7)	19.2 (3.7)	0.340	0.3 (-0.3 to 0.9)	0.373	0.4 (-0.1 to 1.0)	0.144	-0.2 (-0.8 to 0.4)	0.580
Practical reasoning score, adjusted for HAZ at 1 month	18.9 (3.7)	18.7 (3.7)	19.2 (3.7)	0.306	0.3 (-0.3 to 0.9)	0.320	0.4 (-0.1 to 1.0)	0.130	-0.2 (-0.7 to 0.4)	0.615
Practical reasoning score, adjusted for head circumference-for-age z-score at 1 month	18.9 (3.7)	18.8 (3.7)	19.2 (3.7)	0.400	0.3 (-0.3 to 0.9)	0.371	0.4 (-0.2 to 1.0)	0.182	-0.1 (-0.7 to 0.5)	0.668
Practical reasoning score, adjusted for length-for-gestational age	18.9 (3.7)	18.8 (3.7)	19.2 (3.7)	0.324	0.3 (-0.3 to 0.9)	0.307	0.4 (-0.1 to 1.0)	0.143	-0.1 (-0.7 to 0.5)	0.660
Practical reasoning score, adjusted for weight-for-gestational age	18.9 (3.7)	18.8 (3.7)	19.2 (3.7)	0.358	0.3 (-0.3 to 0.8)	0.367	0.4 (-0.1 to 1.0)	0.156	-0.2 (-0.7 to 0.4)	0.612
Practical reasoning score, adjusted for head circumference-for-gestational age	18.9 (3.7)	18.8 (3.7)	19.2 (3.7)	0.418	0.2 (-0.3 to 0.8)	0.417	0.4 (-0.2 to 1.0)	0.188	-0.2 (-0.7 to 0.4)	0.618

[1] SD for multiple imputed data calculated as an average SD from 50 imputations.

Table 8. Total Developmental Score by Intervention Group, Stratified by Duration of Pregnancy at Enrollment

Variable	Interaction test p-value	Control	Monthly SP	AZI-SP	Overall p-value	AZI-SP and control group	p-value	AZI-SP and monthly SP group	p-value	Monthly SP and control group	p-value
Duration of pregnancy at enrollment above median: Total score	0.028	106.9 (18.5)	110.1 (16.8)	113.5 (18.5)	0.005	6.7 (2.6 to 10.7)	0.001	3.5 (-0.4 to 7.3)	0.078	3.2 (-0.8 to 7.2)	0.118
Duration of pregnancy at enrollment at or below median: Total score		110.9 (15.1)	110.5 (17.1)	111.6 (16.6)	0.841	0.7 (-2.9 to 4.2)	0.713	1.1 (-2.6 to 4.8)	0.565	-0.4 (-4.0 to 3.2)	0.815
Maternal height above median: Total score	0.089	107.0 (17.4)	110.1 (16.2)	114.2 (17.1)	0.001	7.1 (3.4 to 10.9)	<0.001	4.0 (0.4 to 7.7)	0.029	3.1 (-0.8 to 7.0)	0.118
Maternal height at or below median: Total score		110.6 (17.7)	110.5 (17.7)	110.6 (18.1)	0.998	0.1 (-3.9 to 4.0)	0.977	0.1 (-3.9 to 4.1)	0.955	-0.1 (-3.8 to 3.7)	0.976

Table 9. Regression Coefficient (95% CI) from Multiple Regression Analysis of Developmental Scores and Explanatory Characteristics

(All models adjusted for intervention group, child sex, and age at time of assessment)

Explanatory variables	Total score			
	Regression coefficient (95% CI), bivariate regression	p-value	Regression coefficient (95% CI), multiple regression	p-value
Constant			29.9 (-200.1 to 259.9)	0.799
Maternal years of schooling	1.0 (0.6 to 1.4)	<0.001	0.7 (0.5 to 1.3)	<0.001
Number of people in the household	-0.3 (-1.0 to 0.4)	0.356	-0.3 (-1.0 to 0.3)	0.335
Asset index	3.1 (2.0 to 4.1)	<0.001	2.3 (1.3 to 3.3)	<0.001
Duration of pregnancy	0.3 (-0.4 to 1.0)	0.334	-0.2 (-1.0 to 0.5)	0.531
HAZ at 1 month	1.8 (0.7 to 2.9)	0.001	-0.4 (-1.7 to 0.9)	0.572
HAZ at 5 years	4.8 (3.5 to 6.1)	<0.001	4.1 (2.8 to 5.5)	<0.001
Head circumference-for-age z-score at 1 month	2.0 (1.0 to 3.0)	<0.001	1.1 (-0.2 to 2.4)	0.095
Head circumference-for-age z-score at 5 years	3.5 (2.2 to 4.7)	<0.001	1.6 (0.2 to 3.1)	0.026

4 Discussion

This study tested the hypothesis that children born to mothers treated with monthly SP with or without two doses of AZI during pregnancy would be larger in size, especially in length/height, at 2 and 5 years of age compared to the children in the control group. The study also tested the hypotheses that children in the AZI-SP and monthly SP groups would have lower mortality during the first 5 years of life, lower morbidity during the first 3 years of life, and higher developmental score at 5 years of age.

Among study infants, absolute length/height and weight were approximately 0.5 cm and 200 g higher in the AZI-SP group compared to the control group throughout the 5 years of follow-up. From 6 to 60 months, the AZI-SP group had 0.13–0.25 higher HAZ compared to the control group. By 5 years of age, the incidence of stunting was about 10 percentage points lower in the AZI-SP group compared to the control group. In this study sample, total mortality from enrollment to 5 years of age was lower in the AZI-SP group compared to the other two intervention groups. Risk of postneonatal death was over two times higher in the control group compared to the AZI-SP group. Child morbidity was similar in all groups during first 3 years of life. Total developmental score at 5 years of age was 3.7 points higher in the AZI-SP group compared to the control group.

The strengths of this trial include random group allocation, broad inclusion criteria, large sample size, comprehensive follow-up, and blinding of the outcome assessors. Internal validity could have been compromised by biased recording of child deaths and NS visits, missing data on anthropometric measurements and developmental items, and some weight measurements rounded to the nearest full kilogram at 36 months and thereafter. However, the caretaker of the child was traced and interviewed if the child did not show up for the next scheduled anthropometric follow-up visit. Also, all deaths were checked and compared against other sources of information before merging the group allocation to mortality data. We therefore believe that we were able to find and record all deaths during the follow-up. Because there were only two health facilities in the study area, we believe it is unlikely that a significant proportion of NS visits were missed. Because the anthropometric and developmental results were robust to sensitivity analyses, we believe missed anthropometric visits, weight measurements rounded to the nearest full kilogram or missing data on developmental items did not significantly bias our conclusions. Hence, we consider the sample findings representative of the population from which the sample was drawn.

We assessed child growth with several outcomes and at several time points. Because of multiple statistical tests, some of our statistically significant results might have been due to chance. However, the results with child length/height and stunting were consistent and showed statistically significant results in favor of the AZI-SP group compared to the control group up to 12 months with HAZ, 36 months with prevalence of stunting, and 60 months with incidence of stunting. The point estimates for length/height in the sample were consistently in favor of the AZI-SP group. Throughout the follow-up period, mean absolute length/height in the AZI-SP group was approximately 0.5 cm higher compared to the control group. Because of this internal consistency, we believe that differences between groups seen at birth were sustained to 5 years of age even though some p-values did not reach a statistically significant level of $p < 0.05$ (Hill 1965). The results for child weight and head circumference showed a similar pattern, but the results were not as consistent as with length/height.

For several age categories the AZI-SP group had lower total mortality compared to the control group, which resulted in lower mortality over the follow-up period; however, only the difference in postneonatal mortality between the AZI-SP and the control group was statistically significant. Infants born preterm or with low birth weight are at higher risk of mortality (Katz et al. 2013, Gladstone et al. 2011). With a

higher prevalence of preterm birth and low birth weight in the control group compared to the AZI-SP group (Luntamo et al. 2010), the mortality results from this study are biologically plausible. However, with a relatively weak association and lack of statistical significance, it is not possible to draw firm conclusions that the intervention had an effect on total mortality. The results are consistent with some mortality effect, but the results are far from being confirmatory.

The association between the intervention and early neonatal deaths was modified by maternal height. Children born to shorter mothers had a higher risk of early neonatal deaths in the AZI-SP group compared to the other two groups. Previous studies have shown that high birth weight and large head size at birth are risk factors for adverse birth outcomes (Pasupathy et al. 2012; Elvander et al. 2012; Mujugira et al. 2013). It is biologically plausible that the combination of increased birth weight and head size in the AZI-SP group along with the small size of the mother could, in turn, lead to complications during delivery. With very limited modern health care available, injuries due to delivery could lead to early neonatal death of the child. Our results also suggest that the association between the intervention and the proportion of miscarriages and stillbirths was modified by maternal BMI. However, among children born to mothers with a BMI above the median, the increase in miscarriages and stillbirths was seen only with the monthly SP group but not with the AZI-SP group, which received the same amount of SP as participants in the monthly SP group. With no logical explanation and a lack of statistical significance, we believe this result might have been due to chance.

We did not see differences between intervention groups in morbidity during the first 3 years. We used NS visits to a health center as a proxy for morbidity in the absence of a more precise measurement of morbidity. However, the number of NS visits to a health center reflects a combination of morbidity, health care seeking, the caretaker's diagnostic ability, and the availability of health care (Aday and Andersen 1974). Because there were only two modern health centers in the study area and health care was provided free for everyone, we believe there were no differences in health-seeking behavior between participants because of the quality of the nearest health center. However, with long distances and lack of transportation it is likely that the child was taken to a health center only for the most severe conditions. Also, this measure of morbidity might be excluding cases of malnutrition as earlier studies in rural India have shown that caretakers are not likely to think of malnutrition as a reason to seek treatment from a health center (Burtscher and Burza 2015; Saito et al. 1997). Although the number of NS visits is most likely underestimated because it describes only the most severe cases of morbidity, we nevertheless believe it does still provide some representation of morbidity. Because of successful randomization and because the children did not receive any intervention during the follow-up period, there is no reason to think there were differences between groups in health care-seeking behavior or in the service they received in the health facility because of group allocation. For this reason we believe that possible differences between groups in number of NS visits would be due to morbidity.

Compared to the control group, the AZI-SP group had a higher total developmental score at 5 years of age. Most of the differences between groups were due to differences in the performance subscale. Because some of the items used in the assessment tool were not appropriate in the Malawian context, we could not make comparisons of child development to international references. However, we validated the use of the sum of passed items retrospectively by using regression analysis. As expected, maternal years of schooling, household asset index, and length/height gain of the child during the follow-up and increase in head circumference during the follow-up were positively associated with the total developmental score (Walker et al. 2005; Yeung et al. 2002; Cheung et al. 2001; Ivanans 1975). Therefore, we consider the results valid and representative of the target population. Descriptive attenuation analysis of the effect of pregnancy outcomes on child development indicated only a small decrease in differences between groups in developmental scores. These findings thus suggest that only part of the differences observed in

development was mediated through the adjustment variable or items associated with it and part was due to a direct and yet uncharacterized effect of the intervention on child development.

Some studies have shown that antenatal nutritional interventions can have a positive effect on development during childhood (Catena et al. 2016; Christian et al. 2010; Dunstan et al. 2008; Helland et al. 2003). Our results on the positive association between preventive antibiotic treatment of pregnant women and subsequent development of their offspring are consistent with those findings. In contrast, a study that prescribed antibiotics to pregnant women who were undergoing a spontaneous preterm labor reported a greater prevalence of functional impairment at 7 years of age among children born to mothers who had been prescribed erythromycin than children born to mothers who did not receive erythromycin (Kenyon et al. 2008). A major design difference between these two trials was that in our LAIS trial, the pregnant women were given antibiotics preventively, in the second trimester, whereas Kenyon and colleagues prescribed daily antibiotics only after the woman was already in spontaneous preterm labor. Although we have no data on it, it seems plausible that antibiotic treatment of women who are already undergoing labor might lead to prolonged exposure of the fetus to infectious agents of an unhealthy intrauterine environment, whereas the preventive approach might have an opposite effect.

We were not able to identify any studies that have tested the effect of antibiotic treatment during pregnancy on child mortality, morbidity, and growth after the neonatal period, although there have been studies that have tested the hypothesis that a nutritional intervention provided to the mother during pregnancy would have positive effects on child growth. Some of these studies, however, suggested that the impact of the nutritional intervention observed at birth is often lost within a year after the child is born (Ashorn et al. 2015; Lanou et al. 2014). And while some studies have reported greater child size or a lower prevalence of stunting among children born to mothers who received nutritional supplementation during pregnancy (Roberfroid et al. 2012; Khan et al. 2011; Vaidya et al. 2008; Kusin et al. 1992), sometimes the effect was seen only with boys and not girls (Khan et al. 2011) or the analysis only included the most adherent participants (Kusin et al. 1992). Because we were not able to identify any studies that followed the growth of children born to mothers who received antibiotics during pregnancy, we were not able to compare our results to a similar study.

Taken together, the results from this study support the hypothesis that differences in child length at 1 month because of provision of monthly SP and two doses of AZI during pregnancy are sustained during the first 5 years of a child's life in rural Malawi. It is also possible that differences in newborn weight and head size are sustained for 5 years, but this was not conclusively confirmed. The results also support a positive effect of the intervention on postneonatal infant mortality and the developmental status of the children at 5 years of age. The results do not support the hypothesis that the intervention would reduce child morbidity during the first 3 years of life in rural areas of Malawi.

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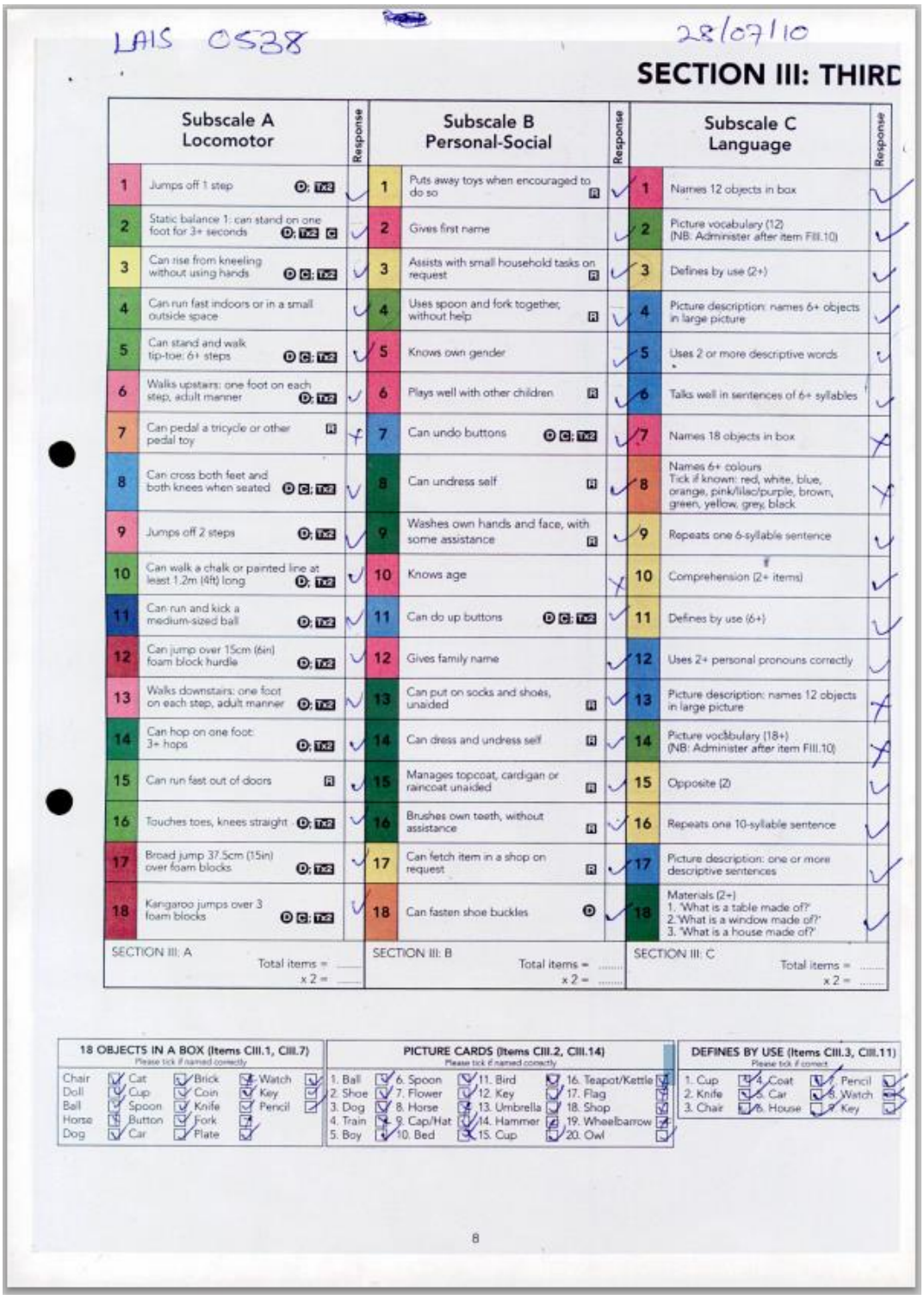
Appendix 1. Griffith's Developmental Assessment Tool for Children 2–8 Years



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SECTION III: THIRD

	Subscale A Locomotor	Response		Subscale B Personal-Social	Response		Subscale C Language	Response
1	Jumps off 1 step D; TX2	✓	1	Puts away toys when encouraged to do so R	✓	1	Names 12 objects in box	✓
2	Static balance 1: can stand on one foot for 3+ seconds D; TX2 C	✓	2	Gives first name	✓	2	Picture vocabulary (12) (NB: Administer after item FIII.10)	✓
3	Can rise from kneeling without using hands D C; TX2	✓	3	Assists with small household tasks on request R	✓	3	Defines by use (2+)	✓
4	Can run fast indoors or in a small outside space	✓	4	Uses spoon and fork together, without help R	✓	4	Picture description: names 6+ objects in large picture	✓
5	Can stand and walk tip-toe: 6+ steps D C; TX2	✓	5	Knows own gender	✓	5	Uses 2 or more descriptive words	✓
6	Walks upstairs: one foot on each step, adult manner D; TX2	✓	6	Plays well with other children R	✓	6	Talks well in sentences of 6+ syllables	✓
7	Can pedal a tricycle or other pedal toy R	✗	7	Can undo buttons D C; TX2	✓	7	Names 18 objects in box	✗
8	Can cross both feet and both knees when seated D C; TX2	✓	8	Can undress self R	✓	8	Names 6+ colours Tick if known: red, white, blue, orange, pink/lilac/purple, brown, green, yellow, grey, black	✗
9	Jumps off 2 steps D; TX2	✓	9	Washes own hands and face, with some assistance R	✓	9	Repeats one 6-syllable sentence	✓
10	Can walk a chalk or painted line at least 1.2m (4ft) long D; TX2	✓	10	Knows age	✗	10	Comprehension (2+ items)	✓
11	Can run and kick a medium-sized ball D; TX2	✓	11	Can do up buttons D C; TX2	✓	11	Defines by use (6+)	✓
12	Can jump over 15cm (6in) foam block hurdle D; TX2	✓	12	Gives family name	✓	12	Uses 2+ personal pronouns correctly	✓
13	Walks downstairs: one foot on each step, adult manner D; TX2	✓	13	Can put on socks and shoes, unaided R	✓	13	Picture description: names 12 objects in large picture	✗
14	Can hop on one foot: 3+ hops D; TX2	✓	14	Can dress and undress self R	✓	14	Picture vocabulary (18+) (NB: Administer after item FIII.10)	✗
15	Can run fast out of doors R	✓	15	Manages topcoat, cardigan or raincoat unaided R	✓	15	Opposite (2)	✓
16	Touches toes, knees straight D; TX2	✓	16	Brushes own teeth, without assistance R	✓	16	Repeats one 10-syllable sentence	✓
17	Broad jump 37.5cm (15in) over foam blocks D; TX2	✓	17	Can fetch item in a shop on request R	✓	17	Picture description: one or more descriptive sentences	✓
18	Kangaroo jumps over 3 foam blocks D C; TX2	✓	18	Can fasten shoe buckles D	✓	18	Materials (2+) 1. 'What is a table made of?' 2. 'What is a window made of?' 3. 'What is a house made of?'	✓
	SECTION III: A Total items = ___ x 2 = ___			SECTION III: B Total items = ___ x 2 = ___			SECTION III: C Total items = ___ x 2 = ___	

18 OBJECTS IN A BOX (Items CIII.1, CIII.7) — Please tick if named correctly

Chair	✓	Cat	✓	Brick	✓	Watch	✓
Doll	✓	Cup	✓	Coin	✓	Key	✓
Ball	✓	Spoon	✓	Knife	✓	Pencil	✓
Horse	✓	Button	✓	Fork	✓		
Dog	✓	Car	✓	Plate	✓		

PICTURE CARDS (Items CIII.2, CIII.14) — Please tick if named correctly

1. Ball	✓	6. Spoon	✓	11. Bird	✓	16. Teapot/Kettle	✓
2. Shoe	✓	7. Flower	✓	12. Key	✓	17. Flag	✓
3. Dog	✓	8. Horse	✓	13. Umbrella	✓	18. Shop	✓
4. Train	✓	9. Cap/Hat	✓	14. Hammer	✓	19. Wheelbarrow	✓
5. Boy	✓	10. Bed	✓	15. Cup	✓	20. Owl	✓

DEFINES BY USE (Items CIII.3, CIII.11) — Please tick if correct

1. Cup	✓	4. Coat	✓	7. Pencil	✓		
2. Knife	✓	5. Car	✓	8. Watch	✓		
3. Chair	✓	6. House	✓	9. Key	✓		

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	Subscale D Eye and Hand Co-ordination	Response		Subscale E Performance	Response		Subscale F Practical Reasoning	Response
1	Builds a tower of 8+ bricks D C; Tx2	✓	1	4-squares board: 50 secs Tx2 C	✓	1	Knows 'penny' or 'money'	✓
2	Copies a horizontal stroke D	✓	2	6-hole board: 50 secs Tx2 C	✓	2	Repeats one digit (8; 2; 7) P	✓
3	Handles scissors: tries to cut D C	✓	3	Returns 9 bricks to box and puts lid on: 50 secs Tx2 C	✓	3	Compares two insets for size	✓
4	Threads 6 beads D C	✓	4	Reassembles screw toy D C; Tx2	✓	4	Repeats 2 digits (1-6; 5-3; 9-4) P	✓
5	Copies a circle: Stage 1 Tx2	✓	5	4-squares board: 40 secs Tx2 C	✓	5	Knows 'big' and 'little'	✓
6	Folds a 10.2cm (4in) square in half D C	✓	6	6-hole board: 40 secs Tx2 C	✓	6	Preliminary counting to 4+	✓
7	Threads 11+ beads D C	✓	7	Assembles brick boxes by colour: all 12 pieces	✓	7	Compares two towers for height	✓
8	Copies a cross: Stage 1	✓	8	11-hole board: 60 secs Tx2 C	✓	8	Compares two lines for length D	✓
9	Draws a person: Stage 1	✓	9	Builds bridge with 3 boxes: inferior model D C	✓	9	Can count 4 bricks correctly Tx2	✓
10	Scissors: can cut a square into two fairly equal halves D C	✓	10	4-squares board: 20 secs Tx2 C	✗	10	Visual memory (3)	✓
11	Folds a 10.2cm (4in) square twice D C	✓	11	Returns 9 bricks to box and puts lid on: 35 secs Tx2 C	✓	11	Compares two weights	✓
12	Copies a ladder: Stage 1	✓	12	6-hole board: 20 secs Tx2 C	✗	12	Knows right from wrong 'Is it right or wrong to hurt someone?' 'Is it right or wrong to lie to someone?'	✓
13	Copies a square: Stage 1	✓	13	Pattern-making No. 2: 50 secs D; P C	✓	13	Can count 10 bricks correctly Tx2	✗
14	Draws a house: Stage 1	✓	14	Train under bridge successfully D C	✓	14	Knows number of fingers on each hand	✓
15	Copies a circle: Stage 2	✓	15	Pattern-making No. 2: 40 secs D; P C	✓	15	Can take out the middle brick	✓
16	Threads 11 beads to colour pattern D C	✗	16	Pattern-making No. 5: 50 secs D; P C	✓	16	Repeats 4 digits (3-7-2-9; 5-8-1-6; 4-9-5-2) P	✗
17	Copies 6+ letters	✗	17	Builds 'gate' to model, using 3 boxes and lids D C	✓	17	Can count 15 bricks correctly Tx2	✗
18	Scissors: can strip edge of paper D C	✗	18	11-hole board: 40 secs Tx2 C	✗	18	'Which costs more?' P C 'A bicycle or a ball?' (practice example) 'A watch or an ice-cream?' (no. 1)	✓
SECTION III: D	Total items = ... x 2 = ...		SECTION III: E	Total items = ... x 2 = ...		SECTION III: F	Total items = ... x 2 = ...	

FORMBOARD	4-squares	6-hole	11-hole
TRIAL 1	32 secs	27 secs	48 secs
TRIAL 2	secs	secs	secs

PATTERN-MAKING	No. 2	No. 3	No. 4	No. 5
TRIAL 1	30 secs	39 secs	37 secs	36 secs

9 BRICKS TO BOX	
TRIAL 1	33 secs
TRIAL 2	secs

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SECTION IV: THIRD

	Subscale A Locomotor	Response		Subscale B Personal-Social	Response		Subscale C Language	Response
1	Can run upstairs	✓	1	Has a special playmate R	✓	1	Comprehension (4+ items)	✓
2	Jump off 3 steps D; TK2	✗	2	Can get a drink of water from the tap or bottle, without assistance R	✓	2	Talks in sentences of 10+ syllables	✓
3	Can bounce and catch a tennis ball D C; TK2	✓	3	Can wash and dry own hands and face, without any assistance R	✓	3	Names 10+ capital letters	✗
4	Hopscotch 1 D C; TK2	✓	4	Can choose own clothes R	✓	4	Similarities (1) P C	✓
5	Can jog at a steady pace all around playground	✓	5	Can shampoo hair, with some assistance R	✓	5	Names 10 colours: red, white, blue, orange, pink/lilac/purple, brown, green, yellow, grey, black	✗
6	Can hopskip, recognisable D C; TK2	✓	6	Knows address	✓	6	Differences (2) P C	✓
7	Can jump over 25cm (10in) foam block hurdle D; TK2	✓	7	Can tie a single knot D C; TK2	✓	7	Names 20+ capital letters	✗
8	Marches in time to tambourine TK2	✓	8	Eats without assistance R	✓	8	Similarities (2) P C	✓
9	Can throw a tennis ball up and catch it D C; TK2	✓	9	Can lay a table completely, with some supervision R	✓	9	Differences (3) P C	✗
10	Runs downstairs	✓	10	Can dress and undress completely, without help R	✓	10	Similarities (3) P C	✗
11	Hopscotch 2 D C; TK2	✓	11	Has one special school friend R	✓	11	Picture description: 3 descriptive sentences	✗
12	Can skip with a rope: 3+ single skips D; TK2	✗	12	Knows full address	✓	12	Repeats one 16-syllable sentence	✗
13	Rides a bicycle (two-wheeler) R	✗	13	Knows birthday 1	✗	13	Names 26 capital letters	✗
14	Static balance 2: can stand on one foot for 20+ seconds D; TK2 C	✓	14	Can tie a bow-knot D C; TK2	✗	14	Uses 6+ descriptive words	✗
15	Hopskips some distance in an open area D C; TK2	✓	15	Can tie own shoelaces R	✗	15	Picture description: 4+ descriptive sentences	✗
16	Hopscotch 3 D C; TK2	✓	16	Can shampoo hair, without any assistance R	✗	16	Comprehension (6+ items)	✗
17	Rides a bicycle (two-wheeler) with skill R	✗	17	Can tie a double bow-knot D C; TK2	✗	17	Differences (4) P C	✗
18	Jumps off 4 steps D; TK2	✗	18	Baths or showers and dries self, without assistance R	✗	18	Uses 6+ personal pronouns correctly	✗
19	Fast skipping with rope: 12+ single skips D; TK2	✗	19	Can lay a table completely, without help or supervision, on all ordinary occasions R	✗	19	Differences (5) P C	✗
20	Skips well with rope: 12+ double skips D; TK2	✗	20	Knows birthday 2	✗	20	Opposites (3)	✗
SECTION IV: A	Total items = ... x 2 = ...		SECTION IV: B	Total items = ... x 2 = ...		SECTION IV: C	Total items = 6 x 2 = ...	

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TO EIGHTH YEARS

	Subscale D Eye and Hand Co-ordination	Response		Subscale E Performance	Response		Subscale F Practical Reasoning	Response
1	Copies 10+ letters	✓	1	Pattern-making No. 5: 40 secs D; P; C	✓	1	Knows number of fingers on both hands together	✓
2	Copies 6+ numbers	✗	2	Pattern-making No. 3: 50 secs D; P; C	✓	2	Can count backwards from 10 D; TX2	✗
3	Can write own first name	✗	3	Returns 9 bricks to box and puts lid on: 20 secs TX2 C	✓	3	Knows morning and afternoon	✓
4	Copies a cross: Stage 2	✓	4	Pattern-making No. 4: 50 secs D; P; C	✓	4	'Which goes faster?' (3) 1. 'A big dog running or a puppy (baby dog) running?' 2. 'A bird flying or an aeroplane?' 3. 'A car or a bicycle?'	✓
5	Copies a triangle: Stage 1	✗	5	Builds bridge with 3 boxes: superior model D C	✓	5	Can say 6 of the 7 days of the week	✗
6	Draws a person: Stage 2	✗	6	4-squares board: 7 secs TX2 C	✗	6	'Which costs more?' P C 'A bicycle or a ball?' (practice example) 'A cold drink or shoes?' (no. 2)	✓
7	Draws a house: Stage 2	✗	7	Pattern-making No. 3: 40 secs D; P; C	✓	7	Can count up to 30	✗
8	Copies 24+ letters	✗	8	Pattern-making No. 2: 25 secs D; P; C	✗	8	Picture arrangement 1: bird on nest P C	✗
9	Copies a window: Stage 1	✓	9	Pattern-making No. 3: 30 secs D; P; C	✗	9	Knows right and left (6+) TX2 1. Right hand 5. Left hand 2. Left ear 6. Right ear 3. Right foot 7. Left foot 4. Right eye 8. Left eye	✓
10	Copies a diamond: Stage 1	✗	10	10-brick memory stairs D C	✗	10	Picture arrangement 2: pouring a drink P C	✗
11	Copies 9 numbers	✗	11	Pattern-making No. 4: 40 secs D; P; C	✓	11	Knows 'long' and 'short'	✓
12	Copies a triangle: Stage 2	✗	12	11-hole board: 30 secs TX2 C	✗	12	Days of the week (2+) 'What day comes after Tuesday?' 'What day comes before Saturday?' 'What day comes after Sunday?'	✓
13	Can write full name	✗	13	Pattern-making No. 2: 20 secs D; P; C	✗	13	Series P C	✓
14	Copies a square: Stage 2	✗	14	6-hole board: 10 secs TX2 C	✗	14	Can count backwards from 20 D; TX2	✗
15	Copies a ladder: Stage 2	✗	15	Pattern-making No. 4: 30 secs D; P; C	✗	15	Knows 'heavy' and 'light'	✓
16	Copies a window: Stage 2	✗	16	Returns 9 bricks to box and puts lid on: 15 secs TX2 C	✗	16	Knows 'high' and 'low'	✓
17	Copies a diamond: Stage 2	✗	17	Pattern-making No. 3: 25 secs D; P; C	✗	17	Repeats 5 digits (6-1-3-8-4; 5-9-2-7-1; 9-2-7-8-6) P	✗
18	Draws a person: Stage 3	✗	18	Pattern-making No. 5: 20 secs D; P; C	✗	18	Repeats 3 digits backwards (1-8-6; 7-2-5; 4-9-3) P	✗
19	Draws a house: Stage 3	✗	19	Pattern-making No. 4: 20 secs D; P; C	✗	19	Picture arrangement 3: building a house P C	✗
20	(Credit as two items) (see DIII.14 & DIV.7)	✓	20	Pattern-making No. 5: 15 secs D; P; C	✗	20	Directional arrows (4)	✓
SECTION IV: D	Total items = ... x 2 = ...		SECTION IV: E	Total items = ... x 2 = ...		SECTION IV: F	Total items = ... x 2 = ...	

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Appendix 2. Supplementary Data Related to Interaction Tests

Supplementary Table 1. P-Values of Interaction Test between Intervention and Maternal and Child Characteristics with Child Mortality Outcomes

	# of previous pregnancies	Maternal malaria at enrollment	Maternal HIV	Maternal height	Maternal BMI at enrollment	Duration of pregnancy at enrollment	Maternal age at enrollment	Child sex	Maternal education at enrollment	Maternal Hb at enrollment
Total number of deaths	0.163	0.847	0.778	0.122	0.250	0.773	0.469	0.619	0.701	0.681
Miscarriages and stillbirths	0.171	0.772	0.313	0.543	0.086	0.996	0.592	0.676	0.284	0.317
Early neonatal deaths	0.666	0.793	0.407	0.007	0.834	0.551	0.928	0.235	0.312	0.524
Postneonatal deaths	0.943	0.501	0.732	0.128	0.394	0.515	0.578	0.796	0.579	0.365
Child deaths	0.764	0.282	0.635	0.497	0.267	0.597	0.676	0.702	0.838	0.725

Supplementary Table 2. P-Values of Interaction Test between Intervention and Maternal and Child Characteristics with Number of NS Visits

	# of previous pregnancies	Maternal malaria at enrollment	Maternal HIV	Maternal height	Maternal BMI at enrollment	Duration of pregnancy at enrollment	Maternal age at enrollment	Child sex	Maternal education at enrollment	Maternal Hb at enrollment
Total number of NS visits during 3 years	0.297	0.041	0.416	0.547	0.333	0.565	0.213	0.181	0.956	0.482
Total number of NS visits during first year	0.151	0.012	0.761	0.877	0.513	0.328	0.118	0.052	0.719	0.294
Total number of NS visits during second year	0.167	0.428	0.120	0.500	0.495	0.348	0.349	0.481	0.190	0.574
Total number of NS visits during third year	0.311	0.052	0.590	0.074	0.493	0.955	0.201	0.268	0.711	0.793

Supplementary Table 3. Incidence of Non-Scheduled Visits by Intervention Group during the First and Third Year of Life, Stratified by Maternal Malaria, Height, and Child Sex

Variable	Interaction test p-value	Control	Monthly SP	AZI-SP	Overall p-value	AZI-SP and control group	P-value	AZI-SP and monthly SP group	P-value	Monthly SP and control group	P-value
Maternal malaria-: NS visits during first 3 years of life	0.041	0.12	0.12	0.13	0.235	1.04 (0.91 to 1.19)	0.528	1.12 (0.98 to 1.27)	0.089	0.94 (0.81 to 1.07)	0.345
Maternal malaria+: NS visits during first 3 years of life		0.13	0.17	0.11	0.139	0.81 (0.56 to 1.17)	0.266	0.61 (0.37 to 1.00)	0.050	1.34 (0.82 to 2.18)	0.241
Maternal malaria-: NS visits during first year of life	0.012	0.25	0.23	0.27	0.106	1.06 (0.94 to 1.21)	0.337	1.15 (1.01 to 1.31)	0.034	0.93 (0.81 to 1.06)	0.276
Maternal malaria+: NS visits during first year of life		0.26	0.36	0.21	0.050	0.81 (0.54 to 1.19)	0.283	0.59 (0.38 to 0.90)	0.016	1.37 (0.94 to 2.00)	0.097
Child sex male: NS visits during first year of life	0.052	0.24	0.24	0.29	0.037	1.21 (1.04 to 1.42)	0.017	1.17 (0.9 to 1.38)	0.060	1.04 (0.87 to 1.23)	0.671
Child sex female: NS visits during first year of life		0.27	0.24	0.24	0.461	0.90 (0.75 to 1.08)	0.263	1.00 (0.83 to 1.21)	1.000	0.90 (0.74 to 1.10)	0.305
Maternal malaria-: NS visits during third year of life	0.052	0.03	0.03	0.04	0.167	1.32 (0.95 to 1.82)	0.099	1.28 (0.94 to 1.76)	0.116	1.02 (0.73 to 1.43)	0.890
Maternal malaria+: NS visits during third year of life		0.01	0.06	0.06	0.023	3.92 (1.31 to 11.71)	0.014	0.97 (0.38 to 2.47)	0.956	4.02 (1.36 to 11.89)	0.012
Maternal height above median: NS visits during third year of life	0.074	0.02	0.04	0.04	0.037	1.72 (1.11 to 2.66)	0.015	1.06 (0.72 to 1.56)	0.759	1.62 (1.04 to 2.52)	0.033
Maternal height at or below median: NS visits during third year of life		0.03	0.02	0.03	0.309	1.14 (0.72 to 1.79)	0.575	1.44 (0.90 to 2.30)	0.128	0.79 (0.49 to 1.27)	0.328

Supplementary Table 4. P-Values of Interaction Test between Intervention and Maternal and Child Characteristics with Growth Outcomes

	# of previous pregnancies	Maternal malaria at enrollment	Maternal HIV	Maternal height	Maternal BMI at enrollment	Duration of pregnancy at enrollment	Maternal age at enrollment	Child sex	Maternal education at enrollment	Maternal Hb at enrollment
HAZ at 24 months	0.918	0.892	0.937	0.205	0.155	0.019	0.220	0.734	0.016	0.061
WAZ at 24 months	0.499	0.195	0.666	0.119	0.269	0.975	0.095	0.772	0.024	0.252
WHZ at 24 months	0.329	0.073	0.627	0.122	0.433	0.148	0.162	0.916	0.175	0.808
MUAC-for-age z-score at 24 months	0.839	0.239	0.491	0.925	0.043	0.999	0.811	0.830	0.390	0.431
Head circumference-for-age z-score at 24 months	0.845	0.822	0.338	0.258	0.585	0.629	0.297	0.408	0.611	0.390
Prevalence HAZ < -2 at 24 months	0.914	0.512	0.838	0.719	0.184	0.003	0.234	0.099	0.021	0.084
Prevalence HAZ < -3 at 24 months	0.959	0.730	0.813	0.508	0.987	0.072	0.184	0.669	0.099	0.009
Prevalence WAZ < -2 at 24 months	0.932	0.207	0.949	0.211	0.476	0.303	0.506	0.459	0.367	0.117
Prevalence WAZ < -3 at 24 months	0.632	0.233	0.336	0.420	0.667	0.100	0.475	0.799	0.359	0.433
Prevalence WHZ < -2 at 24 months	0.322	NA	0.883	0.509	0.744	0.058	0.023	0.158	0.424	0.453
Prevalence MUAC – for-age z-score < -2 at 24 months	0.975	0.779	0.558	0.288	0.030	0.079	0.866	0.848	0.419	0.128
Prevalence head circumference-for-age z-score < -2 at 24 months	0.412	0.684	NA	0.136	0.752	0.146	0.650	0.670	0.214	0.360

Supplementary Table 5. Continuous Growth Outcomes by Intervention Group at 6, 12, 24, 36, 48, and 60 Months of Age, Stratified Analyses

	Outcome	Interaction test p-value	Age	Mean (SD)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value
Education above median	Mean (SD) HAZ	0.016 (with HAZ at 24 months)	6 mo	-1.64 (1.09)	-1.47 (1.26)	-1.24 (1.19)	0.005	0.39 (0.15 to 0.63)	0.001	0.23 (-0.03 to 0.49)	0.081	0.16 (-0.1 to 0.42)	0.217
			12 mo	-1.98 (1.12)	-1.73 (1.17)	-1.55 (1.06)	0.002	0.42 (0.19 to 0.66)	0.000	0.17 (-0.07 to 0.41)	0.154	0.25 (-0.01 to 0.51)	0.057
			24 mo	-2.34 (0.9)	-2.19 (1.09)	-1.94 (1.02)	0.001	0.41 (0.2 to 0.61)	0.000	0.25 (0.02 to 0.49)	0.031	0.15 (-0.08 to 0.38)	0.189
			36 mo	-2.22 (0.93)	-2.00 (1.06)	-1.89 (0.99)	0.009	0.33 (0.12 to 0.54)	0.002	0.1 (-0.13 to 0.33)	0.389	0.22 (-0.01 to 0.46)	0.061
			48 mo	-2.05 (0.9)	-1.88 (1.00)	-1.74 (1.00)	0.016	0.31 (0.1 to 0.52)	0.004	0.14 (-0.09 to 0.36)	0.228	0.17 (-0.05 to 0.39)	0.127
			60 mo	-1.93 (0.90)	-1.70 (0.95)	-1.60 (0.93)	0.006	0.33 (0.13 to 0.54)	0.002	0.11 (-0.11 to 0.32)	0.338	0.23 (0.01 to 0.45)	0.044
Education at or below median	Mean (SD) HAZ		6 mo	-1.37 (1.24)	-1.35 (1.17)	-1.25 (1.32)	0.643	0.12 (-0.14 to 0.38)	0.367	0.09 (-0.16 to 0.35)	0.468	0.03 (-0.21 to 0.27)	0.828
			12 mo	-1.67 (1.13)	-1.74 (1.09)	-1.57 (1.16)	0.353	0.1 (-0.14 to 0.34)	0.402	0.17 (-0.06 to 0.4)	0.150	-0.07 (-0.29 to 0.15)	0.542
			24 mo	-2.04 (1.07)	-2.13 (1.07)	-2.07 (1.08)	0.678	-0.03 (-0.26 to 0.19)	0.772	0.06 (-0.16 to 0.28)	0.582	-0.09 (-0.31 to 0.12)	0.386
			36 mo	-1.90 (0.99)	-2.05 (1.00)	-1.93 (0.97)	0.310	-0.03 (-0.23 to 0.17)	0.768	0.12 (-0.08 to 0.32)	0.252	-0.15 (-0.35 to 0.05)	0.149
			48 mo	-1.77 (0.98)	-1.86 (0.99)	-1.76 (1.06)	0.620	0.01 (-0.21 to 0.23)	0.947	0.09 (-0.13 to 0.31)	0.402	-0.09 (-0.29 to 0.12)	0.404
			60 mo	-1.60 (0.91)	-1.63 (0.94)	-1.62 (0.96)	0.962	-0.02 (-0.22 to 0.18)	0.843	0.01 (-0.2 to 0.21)	0.953	-0.03 (-0.22 to 0.17)	0.789

	Outcome	Interaction test p-value	Age	Mean (SD)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value
Gestational weeks at enrollment above median	Mean (SD) HAZ	0.019 (with HAZ at 24 months)	6 mo	-1.38 (1.17)	-1.31 (1.17)	-1.19 (1.25)	0.314	0.19 (-0.06 to 0.44)	0.131	0.12 (-0.13 to 0.37)	0.341	0.07 (-0.17 to 0.31)	0.574
			12 mo	-1.64 (1.08)	-1.67 (1.13)	-1.54 (1.15)	0.579	0.09 (-0.14 to 0.32)	0.434	0.12 (-0.12 to 0.36)	0.319	-0.03 (-0.26 to 0.2)	0.804
			24 mo	-2.09 (1.03)	-2.18 (1.01)	-2.04 (1.15)	0.507	0.05 (-0.18 to 0.28)	0.683	0.13 (-0.1 to 0.36)	0.259	-0.09 (-0.3 to 0.13)	0.437
			36 mo	-1.95 (0.97)	-2.03 (1.01)	-1.95 (1.09)	0.736	0 (-0.22 to 0.22)	0.993	0.08 (-0.15 to 0.3)	0.505	-0.08 (-0.29 to 0.14)	0.490
			48 mo	-1.82 (0.96)	-1.85 (1.02)	-1.79 (1.11)	0.858	0.03 (-0.19 to 0.25)	0.781	0.06 (-0.16 to 0.29)	0.581	-0.03 (-0.24 to 0.18)	0.755
			60 mo	-1.71 (0.96)	-1.68 (0.93)	-1.64 (1.00)	0.819	0.07 (-0.14 to 0.28)	0.529	0.04 (-0.17 to 0.25)	0.719	0.03 (-0.18 to 0.24)	0.779
Gestational weeks at enrollment at or below median	Mean (SD) HAZ		6 mo	-1.62 (1.18)	-1.49 (1.25)	-1.31 (1.26)	0.050	0.31 (0.06 to 0.57)	0.015	0.19 (-0.07 to 0.44)	0.152	0.13 (-0.13 to 0.38)	0.326
			12 mo	-2.00 (1.17)	-1.8 (1.13)	-1.58 (1.07)	0.002	0.42 (0.18 to 0.66)	0.001	0.22 (-0.01 to 0.45)	0.056	0.2 (-0.05 to 0.44)	0.117
			24 mo	-2.27 (0.98)	-2.14 (1.14)	-1.96 (0.94)	0.015	0.3 (0.1 to 0.51)	0.004	0.18 (-0.04 to 0.39)	0.115	0.12 (-0.1 to 0.35)	0.286
			36 mo	-2.14 (0.96)	-2.02 (1.03)	-1.87 (0.87)	0.028	0.27 (0.07 to 0.46)	0.008	0.15 (-0.05 to 0.35)	0.144	0.12 (-0.1 to 0.34)	0.298
			48 mo	-1.99 (0.94)	-1.88 (0.96)	-1.72 (0.94)	0.037	0.27 (0.06 to 0.49)	0.011	0.16 (-0.04 to 0.37)	0.120	0.11 (-0.11 to 0.33)	0.318
			60 mo	-1.81 (0.88)	-1.65 (0.96)	-1.58 (0.89)	0.075	0.23 (0.03 to 0.43)	0.026	0.06 (-0.14 to 0.27)	0.553	0.16 (-0.05 to 0.38)	0.128

	Outcome	Interaction test p-value	Age	Mean (SD)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value
Hb above median	Mean (SD) HAZ	0.061 (with HAZ at 24 months)	6 mo	-1.39 (1.11)	-1.26 (1.19)	-1.23 (1.33)	0.438	0.16 (-0.1 to 0.41)	0.241	0.03 (-0.24 to 0.29)	0.826	0.13 (-0.12 to 0.37)	0.318
			12 mo	-1.78 (1.05)	-1.64 (1.06)	-1.49 (1.15)	0.058	0.29 (0.05 to 0.52)	0.017	0.16 (-0.08 to 0.39)	0.196	0.13 (-0.09 to 0.36)	0.250
			24 mo	-2.14 (0.97)	-2.07 (1.05)	-2 (1.03)	0.413	0.15 (-0.07 to 0.36)	0.184	0.08 (-0.14 to 0.3)	0.476	0.07 (-0.15 to 0.28)	0.546
			36 mo	-1.98 (0.91)	-1.92 (0.96)	-1.93 (1.01)	0.837	0.05 (-0.16 to 0.26)	0.632	-0.01 (-0.22 to 0.21)	0.957	0.06 (-0.15 to 0.26)	0.588
			48 mo	-1.86 (0.88)	-1.82 (0.96)	-1.74 (1.02)	0.512	0.12 (-0.09 to 0.33)	0.249	0.08 (-0.14 to 0.29)	0.490	0.05 (-0.16 to 0.25)	0.651
			60 mo	-1.72 (0.85)	-1.61 (0.92)	-1.62 (0.94)	0.463	0.1 (-0.1 to 0.3)	0.326	-0.02 (-0.22 to 0.19)	0.876	0.12 (-0.09 to 0.32)	0.259
Hb at or below median	Mean (SD) HAZ		6 mo	-1.59 (1.23)	-1.53 (1.22)	-1.26 (1.18)	0.017	0.33 (0.09 to 0.57)	0.008	0.27 (0.03 to 0.51)	0.029	0.06 (-0.19 to 0.31)	0.652
			12 mo	-1.84 (1.21)	-1.83 (1.18)	-1.63 (1.07)	0.127	0.21 (-0.02 to 0.44)	0.078	0.2 (-0.04 to 0.43)	0.096	0.01 (-0.24 to 0.26)	0.924
			24 mo	-2.2 (1.05)	-2.24 (1.1)	-2.01 (1.07)	0.015	0.3 (0.1 to 0.51)	0.004	0.18 (-0.04 to 0.39)	0.115	0.12 (-0.1 to 0.35)	0.286
			36 mo	-2.1 (1.02)	-2.13 (1.07)	-1.9 (0.95)	0.057	0.2 (0 to 0.41)	0.055	0.23 (0.02 to 0.45)	0.033	-0.03 (-0.25 to 0.19)	0.795
			48 mo	-1.93 (1.01)	-1.91 (1.02)	-1.76 (1.05)	0.271	0.16 (-0.06 to 0.38)	0.144	0.15 (-0.07 to 0.37)	0.181	0.01 (-0.2 to 0.23)	0.904
			60 mo	-1.78 (0.97)	-1.71 (0.96)	-1.6 (0.95)	0.215	0.19 (-0.02 to 0.4)	0.083	0.11 (-0.1 to 0.32)	0.289	0.07 (-0.14 to 0.29)	0.494

	Outcome	Interaction test p-value	Age	Mean (SD)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value
Maternal age above median	Mean (SD) WAZ	0.095 (with WAZ at 24 months)	6 mo	-0.77 (1.15)	-0.81 (1.31)	-0.51 (1.18)	0.036	0.26 (0.02 to 0.51)	0.033	0.3 (0.04 to 0.55)	0.023	-0.03 (-0.29 to 0.23)	0.797
			12 mo	-0.95 (1.09)	-1.01 (1.19)	-0.86 (1.14)	0.478	0.09 (-0.15 to 0.32)	0.461	0.15 (-0.1 to 0.4)	0.230	-0.06 (-0.31 to 0.18)	0.618
			24 mo	-1.28 (0.95)	-1.29 (1.1)	-1.12 (1.03)	0.217	0.16 (-0.05 to 0.38)	0.130	0.17 (-0.05 to 0.4)	0.133	-0.01 (-0.23 to 0.21)	0.948
			36 mo	-1.33 (0.92)	-1.36 (1.01)	-1.19 (1)	0.228	0.14 (-0.06 to 0.35)	0.172	0.17 (-0.04 to 0.39)	0.113	-0.03 (-0.24 to 0.18)	0.796
			48 mo	-1.24 (0.85)	-1.36 (0.92)	-1.25 (1.04)	0.411	-0.01 (-0.22 to 0.19)	0.909	0.11 (-0.1 to 0.33)	0.302	-0.12 (-0.32 to 0.07)	0.214
			60 mo	-1.36 (0.77)	-1.35 (0.84)	-1.23 (0.95)	0.346	0.13 (-0.06 to 0.32)	0.179	0.12 (-0.07 to 0.32)	0.223	0.01 (-0.17 to 0.19)	0.929
Maternal age at or below median	Mean (SD) WAZ		6 mo	-0.8 (1.12)	-0.68 (1.09)	-0.58 (1.13)	0.167	0.22 (-0.01 to 0.44)	0.060	0.1 (-0.13 to 0.32)	0.413	0.12 (-0.1 to 0.35)	0.284
			12 mo	-1.1 (1.14)	-0.88 (1.06)	-0.86 (1.13)	0.094	0.24 (0 to 0.47)	0.050	0.02 (-0.21 to 0.25)	0.851	0.21 (-0.02 to 0.44)	0.067
			24 mo	-1.42 (0.96)	-1.25 (1.04)	-1.37 (1.02)	0.273	0.05 (-0.16 to 0.27)	0.616	-0.12 (-0.34 to 0.1)	0.287	0.17 (-0.04 to 0.39)	0.112
			36 mo	-1.39 (1)	-1.28 (0.99)	-1.39 (0.98)	0.496	0 (-0.21 to 0.21)	0.990	-0.11 (-0.32 to 0.1)	0.299	0.11 (-0.11 to 0.33)	0.312
			48 mo	-1.39 (0.92)	-1.3 (0.94)	-1.31 (0.92)	0.652	0.07 (-0.13 to 0.27)	0.487	-0.02 (-0.22 to 0.18)	0.852	0.09 (-0.11 to 0.29)	0.380
			60 mo	-1.37 (0.78)	-1.33 (0.81)	-1.3 (0.83)	0.750	0.07 (-0.11 to 0.25)	0.454	0.03 (-0.16 to 0.21)	0.774	0.04 (-0.14 to 0.22)	0.647

	Outcome	Interaction test p-value	Age	Mean (SD)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value
Maternal education above median	Mean (SD) WAZ	0.024 (with WAZ at 24 months)	6 mo	-0.85 (1.12)	-0.69 (1.23)	-0.48 (1.12)	0.009	0.36 (0.13 to 0.6)	0.002	0.21 (-0.04 to 0.45)	0.104	0.16 (-0.1 to 0.41)	0.223
			12 mo	-1.16 (1.14)	-0.93 (1.19)	-0.81 (1.13)	0.016	0.35 (0.11 to 0.6)	0.004	0.13 (-0.12 to 0.37)	0.317	0.23 (-0.03 to 0.49)	0.087
			24 mo	-1.5 (0.93)	-1.21 (1.13)	-1.17 (1.04)	0.005	0.34 (0.12 to 0.55)	0.002	0.04 (-0.2 to 0.28)	0.749	0.3 (0.06 to 0.54)	0.015
			36 mo	-1.55 (0.97)	-1.33 (1.07)	-1.27 (1)	0.035	0.28 (0.06 to 0.51)	0.012	0.06 (-0.18 to 0.29)	0.626	0.23 (-0.02 to 0.47)	0.069
			48 mo	-1.51 (0.9)	-1.34 (0.92)	-1.3 (0.91)	0.092	0.22 (0.01 to 0.42)	0.036	0.04 (-0.16 to 0.24)	0.702	0.18 (-0.04 to 0.39)	0.103
			60 mo	-1.44 (0.79)	-1.39 (0.8)	-1.25 (0.89)	0.146	0.18 (-0.01 to 0.37)	0.058	0.14 (-0.06 to 0.33)	0.161	0.04 (-0.15 to 0.23)	0.649
Maternal education at or below median	Mean (SD) WAZ		6 mo	-0.74 (1.14)	-0.79 (1.19)	-0.61 (1.18)	0.339	0.12 (-0.11 to 0.36)	0.299	0.17 (-0.06 to 0.41)	0.152	-0.05 (-0.28 to 0.18)	0.673
			12 mo	-0.92 (1.09)	-0.96 (1.07)	-0.92 (1.14)	0.934	-0.01 (-0.24 to 0.22)	0.959	0.03 (-0.2 to 0.26)	0.781	-0.04 (-0.26 to 0.18)	0.729
			24 mo	-1.23 (0.96)	-1.31 (1.02)	-1.32 (1.03)	0.655	-0.08 (-0.29 to 0.13)	0.436	0 (-0.21 to 0.21)	0.983	-0.08 (-0.28 to 0.12)	0.427
			36 mo	-1.2 (0.92)	-1.31 (0.94)	-1.31 (0.99)	0.457	-0.1 (-0.3 to 0.1)	0.316	0.01 (-0.19 to 0.21)	0.940	-0.11 (-0.3 to 0.08)	0.255
			48 mo	-1.15 (0.85)	-1.32 (0.94)	-1.26 (1.06)	0.179	-0.11 (-0.32 to 0.09)	0.279	0.06 (-0.16 to 0.27)	0.603	-0.17 (-0.36 to 0.01)	0.069
			60 mo	-1.3 (0.76)	-1.3 (0.84)	-1.28 (0.89)	0.953	0.03 (-0.15 to 0.21)	0.774	0.02 (-0.16 to 0.21)	0.794	0 (-0.17 to 0.17)	0.985

	Outcome	Interaction test p-value	Age	Mean (SD)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value
Malaria-	Mean (SD) WHZ < -2	0.073 (with WHZ at 24 months)	6 mo	0.32 (1.17)	0.31 (1.26)	0.4 (1.19)	0.539	0.08 (-0.09 to 0.26)	0.355	0.09 (-0.09 to 0.28)	0.328	-0.01 (-0.19 to 0.18)	0.936
			12 mo	-0.15 (1.04)	-0.1 (1.08)	-0.12 (1.08)	0.778	0.04 (-0.12 to 0.2)	0.634	-0.02 (-0.18 to 0.15)	0.818	0.06 (-0.11 to 0.23)	0.488
			24 mo	-0.28 (1.04)	-0.22 (1.1)	-0.29 (1.03)	0.645	-0.01 (-0.17 to 0.16)	0.944	-0.07 (-0.24 to 0.09)	0.390	0.07 (-0.1 to 0.24)	0.442
			36 mo	-0.29 (1.16)	-0.29 (1.08)	-0.32 (1.01)	0.923	-0.03 (-0.2 to 0.15)	0.747	-0.03 (-0.19 to 0.13)	0.726	0 (-0.18 to 0.18)	0.998
			48 mo	-0.25 (1.12)	-0.35 (1.15)	-0.35 (1.11)	0.509	-0.09 (-0.27 to 0.09)	0.310	0 (-0.18 to 0.18)	0.982	-0.09 (-0.28 to 0.09)	0.313
			60 mo	-0.42 (1.02)	-0.49 (1.03)	-0.43 (1.02)	0.716	0 (-0.17 to 0.16)	0.963	0.06 (-0.11 to 0.23)	0.486	-0.06 (-0.23 to 0.11)	0.469
Malaria+	Mean (SD) WHZ < -2		6 mo	0.07 (1.26)	0.31 (0.94)	0.93 (1.13)	0.039	0.86 (0.19 to 1.52)	0.012	0.62 (0 to 1.23)	0.049	0.24 (-0.3 to 0.78)	0.378
			12 mo	-0.27 (1.23)	-0.12 (1.03)	-0.06 (1.15)	0.822	0.2 (-0.49 to 0.9)	0.563	0.06 (-0.6 to 0.71)	0.860	0.15 (-0.44 to 0.74)	0.625
			24 mo	-0.51 (1.1)	0 (0.96)	0.06 (0.68)	0.056	0.57 (0.08 to 1.06)	0.024	0.06 (-0.41 to 0.53)	0.802	0.51 (0 to 1.02)	0.052
			36 mo	-0.33 (0.77)	0.12 (0.96)	-0.15 (0.94)	0.149	0.17 (-0.35 to 0.7)	0.509	-0.28 (-0.86 to 0.31)	0.347	0.45 (0 to 0.91)	0.052
			48 mo	-0.44 (1.19)	0.1 (1.11)	-0.23 (0.99)	0.219	0.21 (-0.41 to 0.84)	0.504	-0.33 (-0.98 to 0.33)	0.325	0.54 (-0.07 to 1.15)	0.083
			60 mo	-0.65 (1.14)	-0.67 (1.05)	-0.51 (1.06)	0.891	0.14 (-0.53 to 0.8)	0.682	0.16 (-0.53 to 0.84)	0.652	-0.02 (-0.6 to 0.56)	0.949

	Outcome	Interaction test p-value	Age	Mean (SD)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value	Diff. in means (95% CI)	P-value
BMI above median	Mean (SD) MUAC-for-age z-score	0.043 (with MUAC-for-age z-score at 24 months)	6 mo	-0.53 (0.93)	-0.54 (1.13)	-0.34 (1.17)	0.151	0.19 (-0.03 to 0.41)	0.087	0.2 (-0.03 to 0.43)	0.088	-0.01 (-0.23 to 0.2)	0.914
			12 mo	-0.59 (1.01)	-0.52 (0.96)	-0.6 (1.05)	0.695	-0.01 (-0.23 to 0.21)	0.942	-0.08 (-0.29 to 0.13)	0.442	0.07 (-0.14 to 0.28)	0.497
			24 mo	-0.74 (0.86)	-0.56 (0.97)	-0.55 (1.03)	0.105	0.19 (-0.01 to 0.4)	0.063	0.01 (-0.2 to 0.22)	0.905	0.18 (-0.02 to 0.38)	0.077
			36 mo	-0.72 (0.82)	-0.59 (0.94)	-0.62 (0.9)	0.318	0.11 (-0.08 to 0.29)	0.256	-0.03 (-0.22 to 0.16)	0.751	0.14 (-0.05 to 0.33)	0.156
			48 mo	-0.81 (0.86)	-0.79 (0.86)	-0.79 (0.91)	0.991	0.01 (-0.18 to 0.2)	0.910	0 (-0.19 to 0.19)	0.997	0.01 (-0.18 to 0.2)	0.906
			60 mo	-0.95 (0.7)	-0.95 (0.78)	-0.97 (0.88)	0.970	-0.02 (-0.19 to 0.16)	0.854	-0.02 (-0.2 to 0.16)	0.810	0.01 (-0.16 to 0.17)	0.947
BMI at or below median	Mean (SD) MUAC-for-age z-score		6 mo	-0.86 (1.1)	-0.8 (1.1)	-0.7 (1.08)	0.392	0.15 (-0.07 to 0.37)	0.174	0.09 (-0.13 to 0.32)	0.420	0.06 (-0.17 to 0.29)	0.602
			12 mo	-0.99 (1.11)	-0.98 (1.11)	-0.76 (1.18)	0.107	0.23 (-0.01 to 0.47)	0.059	0.22 (-0.02 to 0.47)	0.071	0 (-0.23 to 0.24)	0.967
			24 mo	-0.96 (1.02)	-1.04 (1)	-0.83 (0.95)	0.132	0.13 (-0.08 to 0.33)	0.227	0.21 (0 to 0.42)	0.047	-0.08 (-0.3 to 0.13)	0.444
			36 mo	-0.99 (1)	-0.98 (0.83)	-0.94 (0.88)	0.863	0.05 (-0.15 to 0.26)	0.620	0.04 (-0.14 to 0.23)	0.670	0.01 (-0.19 to 0.21)	0.912
			48 mo	-1.05 (0.78)	-1.1 (0.76)	-1.08 (0.77)	0.825	-0.03 (-0.2 to 0.14)	0.715	0.02 (-0.15 to 0.19)	0.805	-0.05 (-0.22 to 0.11)	0.538
			60 mo	-1.2 (0.76)	-1.23 (0.73)	-1.2 (0.76)	0.949	0 (-0.16 to 0.17)	0.956	0.03 (-0.14 to 0.19)	0.761	-0.02 (-0.19 to 0.14)	0.805

Supplementary Table 6. Prevalence of Various Forms of Undernutrition by Intervention Group at 6, 12, 24, 36, 48, and 60 Months of Age, Stratified Analyses

	Outcome	Interaction test p-value	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Education above median	Prevalence of moderate to severe stunting (HAZ < -2)	0.021 (with stunting at 24 months)	6 mo	38.1% (64/168)	30.9% (51/165)	22.5% (43/191)	0.007	0.59 (0.43 to 0.82)	0.002	0.73 (0.51 to 1.03)	0.076	0.81 (0.6 to 1.1)	0.177
			12 mo	47.7% (73/153)	36.3% (57/157)	31.2% (59/189)	0.006	0.65 (0.5 to 0.86)	0.002	0.86 (0.64 to 1.16)	0.321	0.76 (0.58 to 1)	0.046
			24 mo	70.2% (106/151)	56.6% (86/152)	49.7% (90/181)	0.000	0.71 (0.59 to 0.85)	0.000	0.88 (0.72 to 1.08)	0.212	0.81 (0.68 to 0.96)	0.016
			36 mo	58.1% (86/148)	50% (69/138)	42.5% (77/181)	0.020	0.73 (0.59 to 0.91)	0.005	0.85 (0.67 to 1.08)	0.185	0.86 (0.69 to 1.07)	0.176
			48 mo	48% (72/150)	42.4% (61/144)	38.5% (67/174)	0.226	0.8 (0.62 to 1.03)	0.087	0.91 (0.69 to 1.19)	0.487	0.88 (0.68 to 1.14)	0.339
			60 mo	45.2% (66/146)	39.1% (52/133)	28.5% (47/165)	0.011	0.63 (0.47 to 0.85)	0.003	0.73 (0.53 to 1.01)	0.055	0.86 (0.65 to 1.15)	0.311
Education at or below median	Prevalence of moderate to severe stunting (HAZ < -2)		6 mo	26.2% (50/191)	22.3% (44/197)	26% (47/181)	0.622	0.99 (0.7 to 1.4)	0.963	1.16 (0.81 to 1.66)	0.410	0.85 (0.6 to 1.21)	0.378
			12 mo	39.7% (75/189)	35.9% (69/192)	34.1% (59/173)	0.526	0.86 (0.65 to 1.13)	0.275	0.95 (0.72 to 1.26)	0.714	0.91 (0.7 to 1.17)	0.451
			24 mo	53.5% (100/187)	52.3% (103/197)	52.6% (90/171)	0.972	0.98 (0.81 to 1.2)	0.873	1.01 (0.83 to 1.22)	0.947	0.98 (0.81 to 1.18)	0.816
			36 mo	50.8% (92/181)	48.7% (96/197)	43.9% (76/173)	0.425	0.86 (0.69 to 1.08)	0.196	0.9 (0.72 to 1.13)	0.359	0.96 (0.78 to 1.17)	0.685
			48 mo	39.8% (72/181)	42.5% (79/186)	37.5% (60/160)	0.642	0.94 (0.72 to 1.23)	0.667	0.88 (0.68 to 1.15)	0.350	1.07 (0.84 to 1.37)	0.601
			60 mo	29.6% (50/169)	33.5% (60/179)	33.8% (54/160)	0.662	1.14 (0.83 to 1.57)	0.418	1.01 (0.75 to 1.36)	0.964	1.13 (0.83 to 1.55)	0.432

	Outcome	Interaction test p-value	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Duration of pregnancy at enrollment above median	Prevalence of moderate to severe stunting (HAZ < -2)	0.003 (with stunting at 24 months)	6 mo	24.9% (46/185)	25.1% (44/175)	21.9% (40/183)	0.723	0.88 (0.61 to 1.27)	0.497	0.87 (0.6 to 1.26)	0.464	1.01 (0.71 to 1.45)	0.951
			12 mo	36.9% (66/179)	34.7% (59/170)	32.4% (58/179)	0.675	0.88 (0.66 to 1.17)	0.376	0.93 (0.69 to 1.25)	0.649	0.94 (0.71 to 1.25)	0.674
			24 mo	55.7% (98/176)	57% (98/172)	54.2% (91/168)	0.873	0.97 (0.8 to 1.18)	0.778	0.95 (0.79 to 1.15)	0.603	1.02 (0.85 to 1.23)	0.808
			36 mo	49.4% (84/170)	50% (82/164)	44.8% (78/174)	0.587	0.91 (0.72 to 1.14)	0.395	0.9 (0.72 to 1.12)	0.342	1.01 (0.82 to 1.26)	0.914
			48 mo	38.6% (69/179)	42.3% (71/168)	40.5% (68/168)	0.780	1.05 (0.81 to 1.36)	0.714	0.96 (0.74 to 1.24)	0.740	1.1 (0.85 to 1.42)	0.481
			60 mo	33.1% (54/163)	36.9% (59/160)	31.9% (52/163)	0.614	0.96 (0.7 to 1.32)	0.813	0.87 (0.64 to 1.17)	0.348	1.11 (0.83 to 1.5)	0.481
Duration of pregnancy at enrollment at or below median	Prevalence of moderate to severe stunting (HAZ < -2)		6 mo	39.1% (68/174)	27.3% (51/187)	26.5% (50/189)	0.015	0.68 (0.5 to 0.92)	0.012	0.97 (0.69 to 1.36)	0.859	0.7 (0.52 to 0.95)	0.020
			12 mo	50.3% (82/163)	37.4% (67/179)	32.8% (60/183)	0.002	0.65 (0.5 to 0.84)	0.001	0.88 (0.66 to 1.16)	0.357	0.74 (0.58 to 0.95)	0.018
			24 mo	66.7% (108/162)	51.4% (91/177)	48.4% (89/184)	0.001	0.73 (0.6 to 0.87)	0.001	0.94 (0.76 to 1.16)	0.566	0.77 (0.64 to 0.92)	0.005
			36 mo	59.1% (94/159)	48.5% (83/171)	41.7% (75/180)	0.005	0.7 (0.57 to 0.88)	0.002	0.86 (0.68 to 1.08)	0.200	0.82 (0.67 to 1.01)	0.058
			48 mo	49.3% (75/152)	42.6% (69/162)	35.5% (59/166)	0.049	0.72 (0.55 to 0.94)	0.014	0.83 (0.63 to 1.1)	0.195	0.86 (0.68 to 1.1)	0.237
			60 mo	40.8% (62/152)	34.9% (53/152)	30.3% (49/162)	0.152	0.74 (0.55 to 1.01)	0.054	0.87 (0.63 to 1.2)	0.387	0.85 (0.64 to 1.15)	0.296

	Outcome	Interaction test p-value	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Boys	Prevalence of moderate to severe stunting (HAZ < -2)	0.099 (with stunting at 24 months)	6 mo	36.8% (68/185)	27.4% (54/197)	33.3% (60/180)	0.154	0.91 (0.69 to 1.2)	0.494	1.22 (0.89 to 1.66)	0.216	0.75 (0.55 to 1)	0.054
			12 mo	49.2% (87/177)	40.5% (77/190)	43.3% (77/178)	0.232	0.88 (0.7 to 1.1)	0.267	1.07 (0.84 to 1.36)	0.596	0.82 (0.66 to 1.04)	0.098
			24 mo	63.2% (108/171)	58.6% (112/191)	60.8% (104/171)	0.681	0.96 (0.82 to 1.14)	0.656	1.04 (0.87 to 1.23)	0.674	0.93 (0.79 to 1.1)	0.381
			36 mo	59.2% (97/164)	56% (103/184)	52.6% (90/171)	0.488	0.89 (0.74 to 1.08)	0.231	0.94 (0.78 to 1.14)	0.530	0.95 (0.79 to 1.13)	0.552
			48 mo	47.6% (80/168)	46.3% (81/175)	41.1% (67/163)	0.468	0.86 (0.68 to 1.1)	0.235	0.89 (0.7 to 1.13)	0.342	0.97 (0.77 to 1.22)	0.806
			60 mo	40.2% (66/164)	38.6% (66/171)	39% (62/159)	0.950	0.97 (0.74 to 1.27)	0.819	1.01 (0.77 to 1.33)	0.941	0.96 (0.73 to 1.25)	0.759
Girls	Prevalence of moderate to severe stunting (HAZ < -2)		6 mo	26.4% (46/174)	24.9% (41/165)	15.6% (30/192)	0.034	0.59 (0.39 to 0.9)	0.013	0.63 (0.41 to 0.96)	0.032	0.94 (0.65 to 1.36)	0.742
			12 mo	37% (61/165)	30.8% (49/159)	22.3% (41/184)	0.013	0.6 (0.43 to 0.84)	0.003	0.72 (0.51 to 1.03)	0.075	0.83 (0.61 to 1.13)	0.248
			24 mo	58.7% (98/167)	48.7% (77/158)	42% (76/181)	0.007	0.72 (0.58 to 0.89)	0.002	0.86 (0.68 to 1.09)	0.213	0.83 (0.68 to 1.02)	0.076
			36 mo	49.1% (81/165)	41.1% (62/151)	34.4% (63/183)	0.022	0.7 (0.54 to 0.9)	0.006	0.84 (0.64 to 1.11)	0.212	0.84 (0.65 to 1.07)	0.158
			48 mo	39.3% (64/163)	38.1% (59/155)	35.1% (60/171)	0.724	0.89 (0.67 to 1.18)	0.433	0.92 (0.69 to 1.23)	0.577	0.97 (0.73 to 1.28)	0.828
			60 mo	33.1% (50/151)	32.6% (46/141)	23.5% (39/166)	0.121	0.71 (0.5 to 1.02)	0.061	0.72 (0.5 to 1.04)	0.076	0.99 (0.71 to 1.37)	0.930

	Outcome	Interaction test p-value	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Hb above median	Prevalence of moderate to severe stunting (HAZ < -2)	0.084 (with stunting at 24 months)	6 mo	26.4% (44/167)	20.9% (36/172)	25.1% (45/179)	0.482	0.95 (0.66 to 1.37)	0.799	1.2 (0.82 to 1.77)	0.351	0.79 (0.54 to 1.17)	0.246
			12 mo	40.4% (65/161)	31.4% (54/172)	31.6% (54/171)	0.138	0.78 (0.59 to 1.05)	0.097	1.01 (0.74 to 1.37)	0.971	0.78 (0.58 to 1.04)	0.089
			24 mo	60.4% (96/159)	52.3% (92/176)	52.3% (90/172)	0.220	0.87 (0.72 to 1.05)	0.142	1.00 (0.82 to 1.22)	0.992	0.87 (0.72 to 1.05)	0.138
			36 mo	51% (78/153)	43.1% (72/167)	39.9% (69/173)	0.114	0.78 (0.61 to 1)	0.046	0.93 (0.72 to 1.19)	0.548	0.85 (0.67 to 1.07)	0.163
			48 mo	42.9% (66/154)	38.9% (63/162)	39.6% (65/164)	0.747	0.92 (0.71 to 1.2)	0.561	1.02 (0.78 to 1.34)	0.891	0.91 (0.69 to 1.19)	0.476
			60 mo	35.1% (52/148)	32.4% (48/148)	30.6% (49/160)	0.699	0.87 (0.63 to 1.2)	0.401	0.94 (0.68 to 1.31)	0.734	0.92 (0.67 to 1.27)	0.625
Hb at or below median	Prevalence of moderate to severe stunting (HAZ < -2)		6 mo	36.5% (70/192)	31.1% (59/190)	23.3% (45/193)	0.023	0.64 (0.47 to 0.88)	0.006	0.75 (0.54 to 1.05)	0.093	0.85 (0.64 to 1.13)	0.271
			12 mo	45.9% (83/181)	40.7% (72/177)	33.5% (64/191)	0.056	0.73 (0.57 to 0.94)	0.016	0.82 (0.63 to 1.08)	0.157	0.89 (0.7 to 1.13)	0.328
			24 mo	61.5% (110/179)	56.1% (97/173)	50% (90/180)	0.096	0.81 (0.67 to 0.98)	0.031	0.89 (0.73 to 1.09)	0.255	0.91 (0.76 to 1.09)	0.309
			36 mo	56.8% (100/176)	55.4% (93/168)	46.4% (84/181)	0.121	0.82 (0.67 to 1)	0.051	0.84 (0.68 to 1.03)	0.096	0.97 (0.81 to 1.18)	0.786
			48 mo	44.1% (78/177)	45.8% (77/168)	36.5% (62/170)	0.196	0.83 (0.64 to 1.07)	0.153	0.8 (0.61 to 1.03)	0.083	1.04 (0.82 to 1.32)	0.744
			60 mo	38.3% (64/167)	39% (64/164)	31.5% (52/165)	0.311	0.82 (0.61 to 1.11)	0.198	0.81 (0.6 to 1.09)	0.158	1.02 (0.77 to 1.34)	0.897

	Outcome	Interaction test p-value	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Education above median	Prevalence of severe stunting (HAZ < -3)	0.099 (with severe stunting at 24 months)	6 mo	10.7% (18/168)	9.1% (15/165)	5.2% (10/191)	0.163	0.49 (0.23 to 1.03)	0.059	0.58 (0.27 to 1.25)	0.161	0.85 (0.44 to 1.62)	0.619
			12 mo	15.7% (24/153)	14.7% (23/157)	8.5% (16/189)	0.101	0.54 (0.3 to 0.98)	0.043	0.58 (0.32 to 1.05)	0.074	0.93 (0.55 to 1.58)	0.799
			24 mo	21.2% (32/151)	25% (38/152)	11.6% (21/181)	0.008	0.55 (0.33 to 0.91)	0.020	0.46 (0.28 to 0.76)	0.002	1.18 (0.78 to 1.79)	0.436
			36 mo	19.6% (29/148)	15.2% (21/138)	10.5% (19/181)	0.079	0.54 (0.31 to 0.92)	0.024	0.69 (0.39 to 1.23)	0.208	0.78 (0.46 to 1.3)	0.337
			48 mo	14.7% (22/150)	11.1% (16/144)	8.6% (15/174)	0.248	0.59 (0.31 to 1.1)	0.098	0.78 (0.4 to 1.51)	0.456	0.76 (0.41 to 1.39)	0.372
			60 mo	10.3% (15/146)	7.5% (10/133)	8.5% (14/165)	0.723	0.83 (0.4 to 1.69)	0.599	1.13 (0.52 to 2.45)	0.760	0.73 (0.34 to 1.6)	0.433
Education at or below median	Prevalence of severe stunting (HAZ < -3)		6 mo	8.9% (17/191)	10.2% (20/197)	10.5% (19/181)	0.862	1.18 (0.63 to 2.2)	0.603	1.03 (0.57 to 1.87)	0.912	1.14 (0.62 to 2.11)	0.675
			12 mo	7.9% (15/189)	12.5% (24/192)	11.6% (20/173)	0.328	1.46 (0.77 to 2.76)	0.247	0.92 (0.53 to 1.61)	0.784	1.58 (0.85 to 2.91)	0.147
			24 mo	15.5% (29/187)	21.8% (43/197)	15.8% (27/171)	0.189	1.02 (0.63 to 1.65)	0.942	0.72 (0.47 to 1.12)	0.146	1.41 (0.92 to 2.16)	0.117
			36 mo	12.7% (23/181)	19.8% (39/197)	12.7% (22/173)	0.087	1.00 (0.58 to 1.73)	0.998	0.64 (0.4 to 1.04)	0.072	1.56 (0.97 to 2.5)	0.067
			48 mo	9.4% (17/181)	9.7% (18/186)	8.8% (14/160)	0.956	0.93 (0.47 to 1.83)	0.837	0.9 (0.46 to 1.76)	0.767	1.03 (0.55 to 1.94)	0.926
			60 mo	5.3% (9/169)	7.8% (14/179)	5.6% (9/160)	0.580	1.06 (0.43 to 2.6)	0.905	0.72 (0.32 to 1.62)	0.426	1.47 (0.65 to 3.31)	0.353

	Outcome	Interaction test p-value	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Duration of pregnancy at enrollment above median	Prevalence of severe stunting (HAZ < -3)	0.072 (with severe stunting at 24 months)	6 mo	10.3% (19/185)	7.4% (13/175)	8.2% (15/183)	0.610	0.8 (0.42 to 1.52)	0.494	1.1 (0.54 to 2.25)	0.787	0.72 (0.37 to 1.42)	0.347
			12 mo	10.1% (18/179)	11.2% (19/170)	11.2% (20/179)	0.927	1.11 (0.61 to 2.03)	0.732	1.00 (0.55 to 1.81)	0.999	1.11 (0.6 to 2.05)	0.734
			24 mo	15.3% (27/176)	21.5% (37/172)	16.1% (27/168)	0.257	1.05 (0.64 to 1.71)	0.852	0.75 (0.48 to 1.17)	0.203	1.4 (0.89 to 2.2)	0.141
			36 mo	15.3% (26/170)	17.7% (29/164)	13.2% (23/174)	0.526	0.86 (0.51 to 1.45)	0.583	0.75 (0.45 to 1.24)	0.258	1.16 (0.71 to 1.88)	0.557
			48 mo	10.6% (19/179)	8.9% (15/168)	11.9% (20/168)	0.674	1.12 (0.62 to 2.03)	0.704	1.33 (0.71 to 2.52)	0.375	0.84 (0.44 to 1.6)	0.599
			60 mo	8% (13/163)	7.5% (12/160)	8.6% (14/163)	0.937	1.08 (0.52 to 2.22)	0.841	1.15 (0.55 to 2.4)	0.720	0.94 (0.44 to 2)	0.873
Duration of pregnancy at enrollment at or below median	Prevalence of severe stunting (HAZ < -3)		6 mo	9.2% (16/174)	11.8% (22/187)	7.4% (14/189)	0.353	0.81 (0.41 to 1.6)	0.537	0.63 (0.33 to 1.19)	0.155	1.28 (0.7 to 2.35)	0.427
			12 mo	12.9% (21/163)	15.6% (28/179)	8.7% (16/183)	0.143	0.68 (0.37 to 1.26)	0.218	0.56 (0.31 to 1)	0.049	1.21 (0.72 to 2.05)	0.468
			24 mo	21% (34/162)	24.9% (44/177)	11.4% (21/184)	0.006	0.54 (0.33 to 0.9)	0.017	0.46 (0.28 to 0.74)	0.001	1.18 (0.8 to 1.76)	0.402
			36 mo	16.4% (26/159)	18.1% (31/171)	10% (18/180)	0.089	0.61 (0.35 to 1.08)	0.091	0.55 (0.32 to 0.95)	0.031	1.11 (0.68 to 1.8)	0.675
			48 mo	13.2% (20/152)	11.7% (19/162)	5.4% (9/166)	0.065	0.41 (0.19 to 0.89)	0.023	0.46 (0.22 to 0.99)	0.047	0.89 (0.49 to 1.62)	0.707
			60 mo	7.2% (11/152)	7.9% (12/152)	5.6% (9/162)	0.702	0.77 (0.32 to 1.86)	0.558	0.7 (0.31 to 1.62)	0.409	1.09 (0.48 to 2.48)	0.835

	Outcome	Interaction test p-value	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Hb above median	Prevalence of severe stunting (HAZ < -3)	0.009 (with severe stunting at 24 months)	6 mo	6.6% (11/167)	7.6% (13/172)	8.4% (15/179)	0.819	1.27 (0.6 to 2.69)	0.528	1.11 (0.54 to 2.26)	0.777	1.15 (0.53 to 2.48)	0.727
			12 mo	9.9% (16/161)	11.6% (20/172)	8.2% (14/171)	0.571	0.82 (0.42 to 1.63)	0.579	0.7 (0.37 to 1.35)	0.290	1.17 (0.63 to 2.18)	0.621
			24 mo	18.2% (29/159)	19.9% (35/176)	13.4% (23/172)	0.261	0.73 (0.44 to 1.21)	0.227	0.67 (0.41 to 1.09)	0.107	1.09 (0.7 to 1.7)	0.703
			36 mo	11.8% (18/153)	13.2% (22/167)	12.1% (21/173)	0.923	1.03 (0.57 to 1.86)	0.917	0.92 (0.53 to 1.61)	0.774	1.12 (0.62 to 2.01)	0.704
			48 mo	10.4% (16/154)	9.9% (16/162)	9.2% (15/164)	0.932	0.88 (0.45 to 1.72)	0.709	0.93 (0.47 to 1.81)	0.822	0.95 (0.49 to 1.84)	0.880
			60 mo	6.8% (10/148)	8.8% (13/148)	8.8% (14/160)	0.766	1.3 (0.59 to 2.83)	0.517	1.00 (0.48 to 2.05)	0.992	1.3 (0.59 to 2.87)	0.517
Hb at or below median	Prevalence of severe stunting (HAZ < -3)		6 mo	12.5% (24/192)	11.6% (22/190)	7.3% (14/193)	0.213	0.58 (0.31 to 1.09)	0.090	0.63 (0.33 to 1.19)	0.151	0.93 (0.54 to 1.59)	0.782
			12 mo	12.7% (23/181)	15.3% (27/177)	11.5% (22/191)	0.557	0.91 (0.52 to 1.57)	0.726	0.76 (0.45 to 1.27)	0.293	1.2 (0.72 to 2.01)	0.487
			24 mo	17.9% (32/179)	26.6% (46/173)	13.9% (25/180)	0.010	0.78 (0.48 to 1.26)	0.302	0.52 (0.34 to 0.81)	0.004	1.49 (1 to 2.22)	0.053
			36 mo	19.3% (34/176)	22.6% (38/168)	11.1% (20/181)	0.018	0.57 (0.34 to 0.96)	0.034	0.49 (0.3 to 0.8)	0.005	1.17 (0.77 to 1.78)	0.457
			48 mo	13% (23/177)	10.7% (18/168)	8.2% (14/170)	0.376	0.63 (0.33 to 1.2)	0.162	0.77 (0.4 to 1.49)	0.437	0.82 (0.46 to 1.48)	0.520
			60 mo	8.4% (14/167)	6.7% (11/164)	5.5% (9/165)	0.593	0.65 (0.28 to 1.49)	0.310	0.81 (0.35 to 1.91)	0.635	0.8 (0.37 to 1.74)	0.575

	Outcome	Interaction test p-value	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Duration of pregnancy at enrollment above median	Prevalence of moderate to severe wasting (WHZ < -2)	0.058 (with wasting at 24 months)	6 mo	3.3% (6/184)	3.5% (6/174)	4.4% (8/183)	0.835	1.34 (0.47 to 3.79)	0.580	1.27 (0.45 to 3.58)	0.654	1.06 (0.35 to 3.22)	0.922
			12 mo	5% (9/179)	4.7% (8/169)	5% (9/179)	0.990	1 (0.41 to 2.46)	1.000	1.06 (0.42 to 2.69)	0.899	0.94 (0.37 to 2.39)	0.899
			24 mo	6.9% (12/174)	3.5% (6/170)	5.4% (9/166)	0.390	0.79 (0.34 to 1.82)	0.574	1.54 (0.56 to 4.22)	0.406	0.51 (0.2 to 1.33)	0.170
			36 mo	8.9% (15/168)	6.3% (10/160)	5.8% (10/172)	0.483	0.65 (0.3 to 1.41)	0.276	0.93 (0.4 to 2.18)	0.868	0.7 (0.32 to 1.51)	0.365
			48 mo	4% (7/177)	6.7% (11/164)	5.5% (9/165)	0.534	1.38 (0.53 to 3.62)	0.514	0.81 (0.35 to 1.91)	0.635	1.7 (0.67 to 4.27)	0.263
			60 mo	7.5% (12/160)	5.7% (9/157)	6.3% (10/160)	0.807	0.83 (0.37 to 1.88)	0.659	1.09 (0.45 to 2.61)	0.846	0.76 (0.33 to 1.76)	0.529
Duration of pregnancy at enrollment at or below median	Prevalence of moderate to severe wasting (WHZ < -2)		6 mo	1.2% (2/174)	3.8% (7/186)	1.1% (2/188)	0.143	0.93 (0.13 to 6.51)	0.938	0.28 (0.06 to 1.34)	0.112	3.27 (0.69 to 15.57)	0.136
			12 mo	4.3% (7/162)	5.6% (10/178)	3.8% (7/183)	0.707	0.89 (0.32 to 2.47)	0.816	0.68 (0.26 to 1.75)	0.425	1.3 (0.51 to 3.34)	0.586
			24 mo	3.7% (6/161)	6.9% (12/173)	4.4% (8/180)	0.373	1.19 (0.42 to 3.37)	0.740	0.64 (0.27 to 1.53)	0.315	1.86 (0.72 to 4.84)	0.203
			36 mo	5.1% (8/157)	7.6% (13/171)	4.5% (8/179)	0.430	0.88 (0.32 to 2.41)	0.800	0.59 (0.25 to 1.38)	0.224	1.49 (0.6 to 3.73)	0.392
			48 mo	6.6% (10/152)	8.7% (14/161)	7.8% (13/166)	0.802	1.19 (0.52 to 2.75)	0.683	0.9 (0.44 to 1.86)	0.777	1.32 (0.58 to 3.01)	0.507
			60 mo	6.1% (9/147)	6.8% (10/148)	6.3% (10/158)	0.975	1.03 (0.43 to 2.47)	0.940	0.94 (0.4 to 2.19)	0.880	1.1 (0.46 to 2.63)	0.824

	Outcome	Interaction test p-value	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Age above median	Prevalence of moderate to severe wasting (WHZ < -2)	0.023 (with wasting at 24 months)	6 mo	3.1% (5/163)	3.4% (6/177)	3.2% (6/189)	0.985	1.03 (0.32 to 3.33)	0.954	0.94 (0.31 to 2.85)	0.908	1.11 (0.34 to 3.56)	0.867
			12 mo	3.6% (6/167)	5.5% (9/165)	4.4% (8/181)	0.717	1.23 (0.44 to 3.47)	0.696	0.81 (0.32 to 2.05)	0.657	1.52 (0.55 to 4.17)	0.418
			24 mo	6.3% (10/160)	6.4% (11/173)	3.4% (6/176)	0.399	0.55 (0.2 to 1.47)	0.230	0.54 (0.2 to 1.42)	0.209	1.02 (0.44 to 2.33)	0.968
			36 mo	8.5% (13/153)	8.9% (15/168)	3.4% (6/176)	0.102	0.4 (0.16 to 1.03)	0.058	0.38 (0.15 to 0.96)	0.041	1.05 (0.52 to 2.14)	0.891
			48 mo	5.7% (9/157)	9.5% (15/158)	6.6% (11/168)	0.402	1.14 (0.49 to 2.68)	0.760	0.69 (0.33 to 1.46)	0.330	1.66 (0.75 to 3.68)	0.215
			60 mo	7.5% (11/147)	8.6% (13/151)	6.2% (10/162)	0.714	0.82 (0.36 to 1.89)	0.649	0.72 (0.32 to 1.59)	0.412	1.15 (0.53 to 2.49)	0.722
Age at or below median	Prevalence of moderate to severe wasting (WHZ < -2)		6 mo	1.5% (3/195)	3.8% (7/183)	2.2% (4/182)	0.365	1.43 (0.32 to 6.31)	0.638	0.57 (0.17 to 1.93)	0.370	2.49 (0.65 to 9.48)	0.182
			12 mo	5.8% (10/174)	5% (9/182)	4.4% (8/181)	0.848	0.77 (0.31 to 1.91)	0.571	0.89 (0.35 to 2.27)	0.813	0.86 (0.36 to 2.07)	0.737
			24 mo	4.6% (8/175)	4.1% (7/170)	6.5% (11/170)	0.577	1.42 (0.58 to 3.44)	0.443	1.57 (0.63 to 3.95)	0.336	0.9 (0.33 to 2.42)	0.836
			36 mo	5.8% (10/172)	4.9% (8/163)	6.9% (12/175)	0.750	1.18 (0.5 to 2.77)	0.705	1.4 (0.59 to 3.33)	0.451	0.84 (0.33 to 2.17)	0.725
			48 mo	4.7% (8/172)	6% (10/167)	6.8% (11/163)	0.742	1.45 (0.56 to 3.74)	0.441	1.13 (0.49 to 2.58)	0.778	1.29 (0.49 to 3.38)	0.608
			60 mo	6.3% (10/160)	3.9% (6/154)	6.4% (10/156)	0.566	1.03 (0.44 to 2.39)	0.953	1.65 (0.61 to 4.42)	0.324	0.62 (0.23 to 1.67)	0.348

	Outcome	Interaction test p-value	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
BMI above median	Prevalence of low MUAC (MUAC-for-age z-score < -2)	0.030 (with low MUAC at 24 months)	6 mo	7.8% (13/167)	8.5% (16/189)	7.3% (14/192)	0.912	0.94 (0.45 to 1.94)	0.860	0.86 (0.43 to 1.71)	0.670	1.09 (0.54 to 2.19)	0.815
			12 mo	5.6% (9/162)	8.7% (16/184)	9.7% (18/186)	0.362	1.74 (0.8 to 3.77)	0.159	1.11 (0.57 to 2.16)	0.751	1.57 (0.7 to 3.5)	0.276
			24 mo	8.8% (14/159)	6.6% (12/181)	7.8% (14/180)	0.765	0.88 (0.42 to 1.84)	0.740	1.17 (0.56 to 2.46)	0.673	0.75 (0.35 to 1.61)	0.465
			36 mo	5.1% (8/157)	7.4% (13/175)	7.2% (13/181)	0.655	1.41 (0.6 to 3.32)	0.432	0.97 (0.46 to 2.03)	0.929	1.46 (0.62 to 3.43)	0.388
			48 mo	8.5% (13/153)	7.7% (13/169)	9.9% (17/171)	0.759	1.17 (0.59 to 2.33)	0.655	1.29 (0.65 to 2.58)	0.467	0.91 (0.43 to 1.89)	0.792
			60 mo	5.5% (8/145)	6.4% (10/156)	9.9% (16/162)	0.303	1.79 (0.79 to 4.06)	0.164	1.54 (0.72 to 3.29)	0.265	1.16 (0.47 to 2.87)	0.745
BMI at or below median	Prevalence of low MUAC (MUAC-for-age z-score < -2)		6 mo	13.9% (27/195)	12% (21/175)	8.8% (16/182)	0.313	0.63 (0.35 to 1.14)	0.128	0.73 (0.4 to 1.36)	0.323	0.87 (0.51 to 1.48)	0.599
			12 mo	17% (31/182)	19.4% (32/165)	15.4% (27/175)	0.624	0.91 (0.57 to 1.45)	0.681	0.8 (0.5 to 1.27)	0.336	1.14 (0.73 to 1.78)	0.568
			24 mo	12.9% (23/178)	16.6% (28/169)	9.9% (17/171)	0.200	0.77 (0.43 to 1.39)	0.385	0.6 (0.34 to 1.06)	0.076	1.28 (0.77 to 2.14)	0.340
			36 mo	15% (26/173)	10.6% (17/160)	11.1% (19/172)	0.407	0.74 (0.42 to 1.29)	0.282	1.04 (0.56 to 1.93)	0.902	0.71 (0.4 to 1.26)	0.241
			48 mo	11.8% (21/178)	12.4% (20/161)	11.7% (19/162)	0.978	0.99 (0.55 to 1.8)	0.985	0.94 (0.52 to 1.7)	0.848	1.05 (0.59 to 1.89)	0.863
			60 mo	12.9% (21/163)	12.3% (19/154)	12.6% (20/159)	0.990	0.98 (0.54 to 1.75)	0.936	1.02 (0.57 to 1.84)	0.949	0.96 (0.53 to 1.73)	0.886

	Outcome	Interaction test p-value	Age	% (Number of outcomes/infants with outcome data)				Comparison between AZI-SP and control group		Comparison between AZI-SP and monthly SP group		Comparison between monthly SP and control group	
				Control	Monthly SP	AZI-SP	Overall p-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value	Risk ratio (95% CI)	P-value
Duration of pregnancy at enrollment above median	Prevalence of low MUAC (MUAC-for-age z-score < -2)	0.079 (with low MUAC at 24 months)	6 mo	13.8% (26/188)	10.2% (18/177)	8.7% (16/185)	0.260	0.63 (0.35 to 1.13)	0.118	0.85 (0.45 to 1.62)	0.621	0.74 (0.42 to 1.29)	0.286
			12 mo	11.7% (21/180)	15.9% (27/170)	10.6% (19/179)	0.296	0.91 (0.51 to 1.63)	0.752	0.67 (0.39 to 1.16)	0.150	1.36 (0.8 to 2.31)	0.255
			24 mo	12.6% (22/175)	9.9% (17/172)	10.7% (18/168)	0.716	0.85 (0.47 to 1.53)	0.593	1.08 (0.58 to 2.03)	0.801	0.79 (0.43 to 1.43)	0.430
			36 mo	11.7% (20/171)	7.9% (13/164)	9.8% (17/174)	0.516	0.84 (0.45 to 1.54)	0.564	1.23 (0.62 to 2.46)	0.553	0.68 (0.35 to 1.32)	0.252
			48 mo	9.5% (17/179)	9.5% (16/168)	11.9% (20/168)	0.703	1.25 (0.68 to 2.31)	0.469	1.25 (0.67 to 2.33)	0.482	1 (0.52 to 1.92)	0.993
			60 mo	10.6% (17/160)	10.6% (17/161)	8.1% (13/161)	0.685	0.76 (0.38 to 1.51)	0.435	0.76 (0.38 to 1.52)	0.445	0.99 (0.53 to 1.88)	0.985
Duration of pregnancy at enrollment at or below median	Prevalence of low MUAC (MUAC-for-age z-score < -2)		6 mo	8.1% (14/174)	10.2% (19/187)	7.4% (14/190)	0.601	0.92 (0.45 to 1.87)	0.809	0.73 (0.38 to 1.4)	0.339	1.26 (0.65 to 2.44)	0.487
			12 mo	11.6% (19/164)	11.7% (21/179)	14.2% (26/183)	0.705	1.23 (0.71 to 2.13)	0.468	1.21 (0.7 to 2.1)	0.495	1.01 (0.56 to 1.83)	0.967
			24 mo	9.3% (15/162)	12.9% (23/178)	7.1% (13/184)	0.173	0.76 (0.37 to 1.59)	0.469	0.55 (0.29 to 1.04)	0.068	1.4 (0.74 to 2.64)	0.305
			36 mo	8.8% (14/159)	9.9% (17/171)	8.3% (15/180)	0.866	0.95 (0.46 to 1.95)	0.881	0.84 (0.43 to 1.63)	0.602	1.13 (0.56 to 2.27)	0.733
			48 mo	11.2% (17/152)	10.5% (17/162)	9.6% (16/166)	0.907	0.86 (0.44 to 1.67)	0.660	0.92 (0.48 to 1.76)	0.797	0.94 (0.49 to 1.8)	0.848
			60 mo	8.1% (12/148)	8.1% (12/149)	14.3% (23/161)	0.126	1.76 (0.88 to 3.53)	0.110	1.77 (0.91 to 3.44)	0.090	0.99 (0.45 to 2.21)	0.987

Supplementary Table 7. P-Values of Interaction Test between Intervention and Maternal and Child Characteristics with Total Developmental Score

	# of previous pregnancies	Maternal malaria at enrollment	Maternal HIV	Maternal height	Maternal BMI at enrollment	Duration of pregnancy at enrollment	Maternal age at enrollment	Child sex	Maternal education at enrollment	Maternal Hb at enrollment
Total developmental score	0.188	0.929	0.863	0.089	0.467	0.028	0.679	0.212	0.686	0.156

Appendix 3. Comparison of Original and Multiple Imputation Data

Supplementary Table 8. Continuous Growth Outcomes by Child Sex at 6, 12, 24, 36, 48, and 60 Months of Age

Outcome	Original data (not imputed)				Multiple imputation with interval censoring for weight measurements at full kg done at or after 36 months[2]				Multiple imputed data for missing values[2]			
		Child sex				Child sex				Child sex		
	Age	Male	Female	N	Age	Male	Female	N	Age	Male	Female	N
Mean (SD) age at measurement (months)	6 mo	6.1 (0.2)	6.1 (0.2)	1,105								
	12 mo	12.1 (0.2)	12.1 (0.2)	1,055								
	24 mo	24.2 (0.4)	24.2 (0.4)	1,040								
	36 mo	36.1 (0.2)	36.1 (0.3)	1,019								
	48 mo	48.1 (0.2)	48.1 (0.3)	995								
	60 mo	60.1 (0.3)	60.1 (0.3)	953								
Mean (SD) length/height (cm)	6 mo	64.5 (2.8)	63.1 (2.6)	1,093					6 mo	64.5 (2.7)	63.1 (2.6)	1,210
	12 mo	71.3 (2.8)	70.3 (2.6)	1,053					12 mo	71.3 (2.8)	70.2 (2.6)	1,189
	24 mo	81.0 (3.3)	80.2 (3.2)	1,039					24 mo	81.0 (3.2)	80.1 (3.2)	1,160
	36 mo	88.3 (3.8)	88.0 (3.6)	1,018					36 mo	88.3 (3.7)	87.9 (3.6)	1,143
	48 mo	95.3 (4.2)	95.2 (4.2)	995					48 mo	95.4 (4.2)	95.3 (4.2)	1,136
	60 mo	101.8 (4.4)	102.0 (4.3)	952					60 mo	101.8 (4.4)	101.9 (4.3)	1,131
Mean (SD) weight (kg)	6 mo	7.4 (1.0)	6.9 (0.9)	1,101	6 mo	7.4 (1.0)	6.9 (0.9)	1,101	6 mo	7.3 (1.0)	6.9 (0.9)	1,210
	12 mo	8.6 (1.1)	8.2 (1.1)	1,052	12 mo	8.6 (1.1)	8.2 (1.1)	1,052	12 mo	8.6 (1.1)	8.2 (1.0)	1,189
	24 mo	10.5 (1.2)	10.1 (1.3)	1,025	24 mo	10.5 (1.2)	10.1 (1.3)	1,025	24 mo	10.5 (1.2)	10.1 (1.3)	1,160
	36 mo	12.2 (1.4)	11.9 (1.5)	1,008	36 mo	12.2 (1.4)	11.9 (1.4)	1,008	36 mo	12.2 (1.4)	11.9 (1.4)	1,143
	48 mo	14.0 (1.6)	13.6 (1.7)	985	48 mo	14.0 (1.6)	13.6 (1.7)	985	48 mo	14.0 (1.6)	13.6 (1.7)	1,136
	60 mo	15.5 (1.7)	15.2 (1.8)	944	60 mo	15.5 (1.7)	15.2 (1.8)	944	60 mo	15.5 (1.7)	15.2 (1.8)	1,131
Mean (SD) head circumference (cm)	6 mo	43.6 (1.5)	42.6 (1.4)	1,097					6 mo	43.6 (1.4)	42.6 (1.4)	1,210
	12 mo	45.9 (1.5)	44.8 (1.4)	1,048					12 mo	45.9 (1.5)	44.8 (1.3)	1,189
	24 mo	47.9 (1.4)	46.8 (1.4)	1,038					24 mo	47.9 (1.4)	46.9 (1.3)	1,160
	36 mo	49.0 (1.4)	47.8 (1.3)	1,016					36 mo	48.9 (1.4)	47.8 (1.3)	1,143
	48 mo	49.6 (1.3)	48.5 (1.3)	994					48 mo	49.6 (1.4)	48.5 (1.3)	1,136
	60 mo	49.9 (1.4)	48.8 (1.4)	948					60 mo	49.9 (1.4)	48.8 (1.4)	1,131

Outcome	Original data (not imputed)				Multiple imputation with interval censoring for weight measurements at full kg done at or after 36 months[2]				Multiple imputed data for missing values[2]			
		Child sex				Child sex				Child sex		
	Age	Male	Female	N	Age	Male	Female	N	Age	Male	Female	N
Mean (SD) MUAC (cm)	6 mo	13.6 (1.2)	13.2 (1.2)	1,101					6 mo	13.5 (1.2)	13.2 (1.2)	1,210
	12 mo	13.8 (1.2)	13.5 (1.2)	1,055					12 mo	13.8 (1.2)	13.5 (1.2)	1,189
	24 mo	14.3 (1.1)	14.1 (1.1)	1,039					24 mo	14.3 (1.1)	14.1 (1.1)	1,160
	36 mo	14.8 (1.0)	14.7 (1.1)	1,019					36 mo	14.8 (1.1)	14.7 (1.1)	1,143
	48 mo	15.0 (1.0)	15.0 (1.1)	995					48 mo	15.0 (1.0)	15.0 (1.1)	1,136
	60 mo	15.2 (1.0)	15.2 (1.1)	953					60 mo	15.2 (1.0)	15.2 (1.1)	1,131
Mean (SD) height-for-age z-score	6 mo	-1.52 (1.28)	-1.23 (1.13)	1,093					6 mo	-1.52 (1.27)	-1.23 (1.13)	1,210
	12 mo	-1.90 (1.19)	-1.49 (1.01)	1,053					12 mo	-1.89 (1.18)	-1.50 (1.02)	1,189
	24 mo	-2.26 (1.07)	-1.95 (1.00)	1,039					24 mo	-2.24 (1.06)	-1.96 (0.99)	1,160
	36 mo	-2.11 (1.02)	-1.87 (0.95)	1,018					36 mo	-2.11 (1.01)	-1.89 (0.95)	1,143
	48 mo	-1.92 (1.00)	-1.75 (0.98)	995					48 mo	-1.91 (1.00)	-1.75 (0.96)	1,136
	60 mo	-1.77 (0.95)	-1.57 (0.91)	952					60 mo	-1.76 (0.95)	-1.58 (0.90)	1,131
Mean (SD) weight-for-age z-score	6 mo	-0.79 (1.21)	-0.58 (1.12)	1,101	6 mo	-0.79 (1.21)	-0.58 (1.12)	1,101	6 mo	-0.81 (1.20)	-0.60 (1.11)	1,210
	12 mo	-1.10 (1.16)	-0.77 (1.06)	1,052	12 mo	-1.10 (1.16)	-0.77 (1.06)	1,052	12 mo	-1.10 (1.15)	-0.80 (1.05)	1,189
	24 mo	-1.39 (1.02)	-1.19 (1.02)	1,025	24 mo	-1.39 (1.02)	-1.19 (1.02)	1,024	24 mo	-1.37 (1.00)	-1.19 (1.01)	1,160
	36 mo	-1.38 (0.98)	-1.27 (0.98)	1,008	36 mo	-1.38 (0.98)	-1.27 (0.98)	1,008	36 mo	-1.38 (0.98)	-1.28 (0.97)	1,143
	48 mo	-1.31 (0.93)	-1.30 (0.94)	985	48 mo	-1.31 (0.92)	-1.30 (0.93)	985	48 mo	-1.30 (0.93)	-1.32 (0.93)	1,136
	60 mo	-1.30 (0.82)	-1.35 (0.85)	944	60 mo	-1.30 (0.81)	-1.35 (0.85)	944	60 mo	-1.30 (0.82)	-1.35 (0.85)	1,131
Mean (SD) weight-for-height z-score	6 mo	0.31 (1.24)	0.38 (1.16)	1,089	6 mo	0.31 (1.24)	0.38 (1.16)	1,089	6 mo	0.29 (1.25)	0.35 (1.17)	1,210
	12 mo	-0.20 (1.11)	-0.04 (1.03)	1,050	12 mo	-0.20 (1.11)	-0.04 (1.03)	1,050	12 mo	-0.20 (1.10)	-0.06 (1.02)	1,189
	24 mo	-0.31 (1.08)	-0.20 (1.02)	1,024	24 mo	-0.30 (1.07)	-0.19 (1.03)	1,024	24 mo	-0.28 (1.07)	-0.17 (1.03)	1,160
	36 mo	-0.29 (1.08)	-0.27 (1.05)	1,007	36 mo	-0.29 (1.07)	-0.28 (1.05)	1,007	36 mo	-0.31 (1.10)	-0.27 (1.05)	1,143
	48 mo	-0.26 (1.18)	-0.36 (1.07)	985	48 mo	-0.26 (1.16)	-0.36 (1.05)	984	48 mo	-0.25 (1.19)	-0.41 (1.08)	1,136
	60 mo[1]	-0.36 (1.01)	-0.57 (1.03)	930	60 mo[1]	-0.36 (1.00)	-0.57 (1.02)	930	60 mo	-0.37 (1.03)	-0.56 (1.03)	1,131
Mean (SD) head circumference-for-age z-score	6 mo	0.16 (1.18)	0.26 (1.08)	1,097					6 mo	0.15 (1.17)	0.26 (1.07)	1,210
	12 mo	-0.18 (1.16)	-0.07 (1.01)	1,048					12 mo	-0.18 (1.16)	-0.07 (1.00)	1,189
	24 mo	-0.24 (1.04)	-0.24 (0.97)	1,038					24 mo	-0.25 (1.02)	-0.24 (0.95)	1,160
	36 mo	-0.36 (0.99)	-0.48 (0.94)	1,016					36 mo	-0.38 (0.99)	-0.48 (0.93)	1,143
	48 mo	-0.44 (0.92)	-0.57 (0.94)	994					48 mo	-0.43 (0.94)	-0.56 (0.92)	1,136
	60 mo[1]	-0.53 (0.95)	-0.77 (0.98)	935					60 mo	-0.55 (0.96)	-0.77 (0.97)	1,131

Outcome	Original data (not imputed)				Multiple imputation with interval censoring for weight measurements at full kg done at or after 36 months[2]				Multiple imputed data for missing values[2]			
	Age	Child sex		N	Age	Child sex		N	Age	Child sex		N
		Male	Female			Male	Female			Male	Female	
Mean (SD) MUAC-for-age z-score	6 mo	-0.69 (1.13)	-0.56 (1.08)	1,101					6 mo	-0.70 (1.13)	-0.57 (1.08)	1,210
	12 mo	-0.81 (1.11)	-0.65 (1.05)	1,055					12 mo	-0.81 (1.10)	-0.66 (1.05)	1,189
	24 mo	-0.83 (1.00)	-0.71 (0.98)	1,039					24 mo	-0.83 (0.99)	-0.70 (0.98)	1,160
	36 mo	-0.80 (0.90)	-0.80 (0.93)	1,019					36 mo	-0.82 (0.91)	-0.81 (0.92)	1,143
	48 mo	-0.91 (0.81)	-0.96 (0.86)	995					48 mo	-0.90 (0.82)	-0.96 (0.85)	1,136
	60 mo[1]	-1.02 (0.78)	-1.15 (0.77)	940					60 mo	-1.02 (0.78)	-1.15 (0.78)	1,131

[1] Z-scores calculated only for children < 61 months of age. Participants included in the analysis allowed to be up to 62 months.

[2] SD for multiple imputed data calculated as an average SD from 50 imputations

Supplementary Table 9. Developmental Scores by Child Sex at 60 Months of Age

Outcome	Original data (not imputed)			Multiple imputed data for missing values[1]		
	Child sex			Child sex		
	Male	Female	N	Male	Female	N
Mean (SD) total developmental score	110.0 (17.8)	108.5 (17.0)	667	111.1 (17.1)	110.0 (17.5)	1,134
Locomotor score	24.5 (4.1)	24.8 (3.3)	913	24.7 (4.1)	24.9 (4.5)	1,134
Personal-social score	27.1 (3.9)	27.3 (4.0)	902	27.1 (3.9)	27.3 (4.0)	1,134
Language score	15.0 (4.7)	14.8 (5.2)	914	15.2 (4.8)	14.9 (5.2)	1,134
Eye and hand coordination score	8.8 (3.0)	8.3 (3.2)	909	9.0 (3.1)	8.5 (3.3)	1,134
Performance score	15.8 (6.1)	14.4 (6.0)	813	16.3 (6.1)	15.3 (6.1)	1,134
Practical reasoning score	18.8 (3.6)	19.0 (3.8)	912	18.9 (3.7)	19.0 (3.8)	1,134

[1] SD for multiple imputed data calculated as an average SD from 50 imputations.